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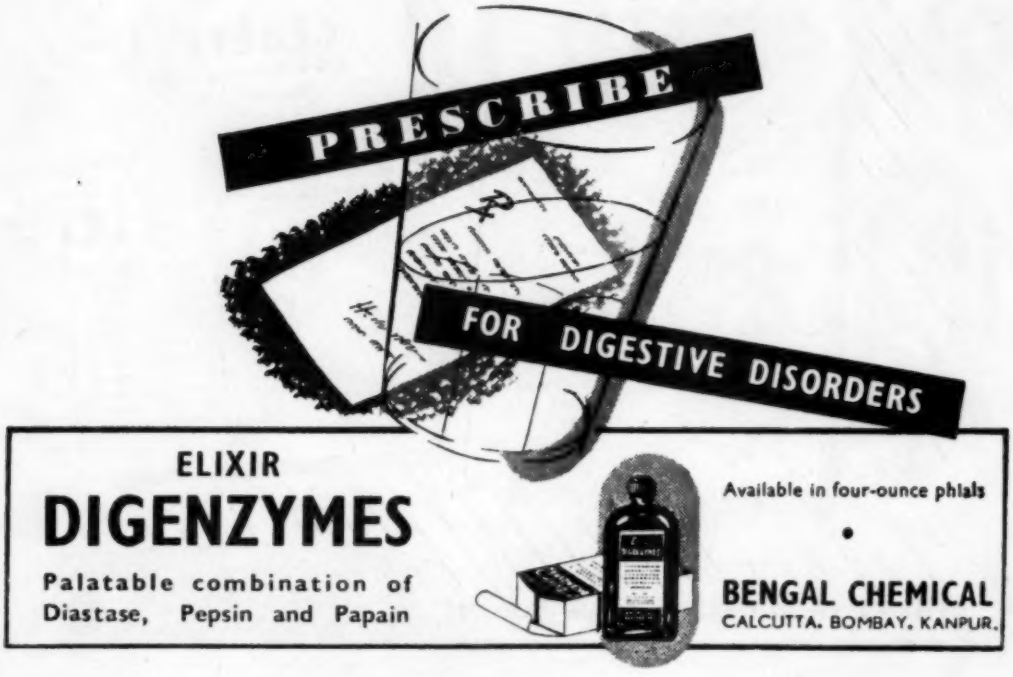

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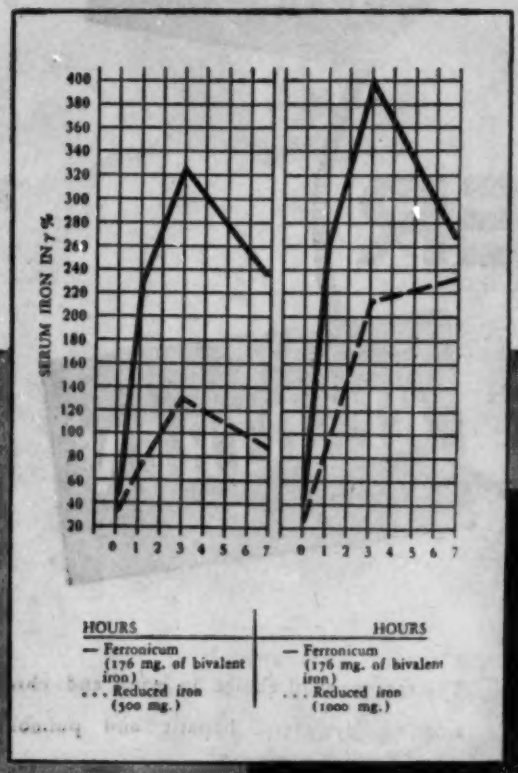

The graph shows the better absorption of Ferronicum as compared to reduced iron. Small oral doses of Ferronicum increase the serum iron level far more than large doses of reduced iron (average from 5 patients). (Jasinsky. Schw. Med. Wschr., 80, 59, 1950)

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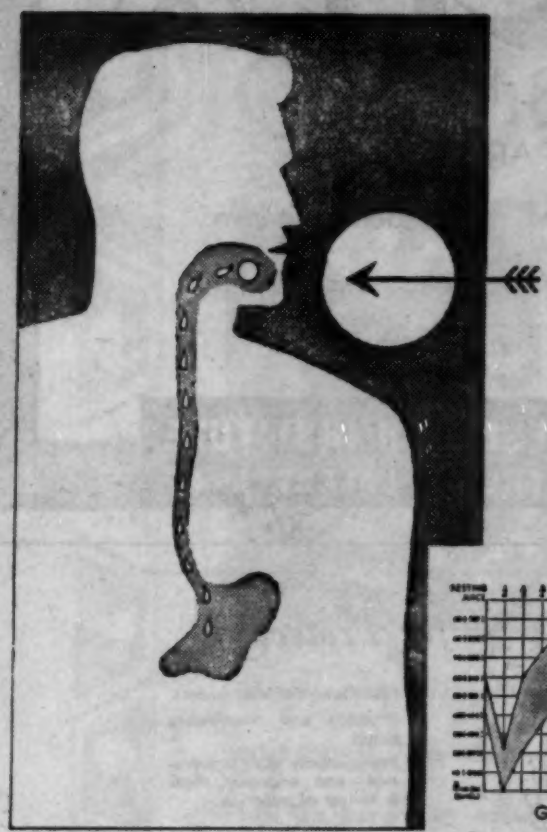

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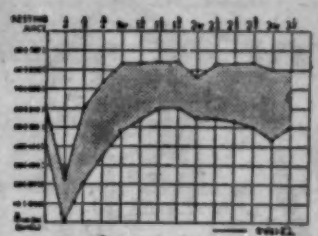
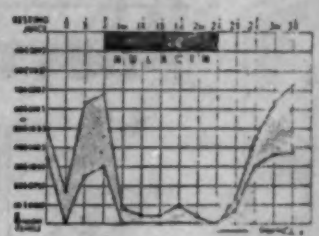


Gastric Analysis

Superimposed gruel fractional test-meal curves of five cases of duodenal ulcer.



Gastric Analysis

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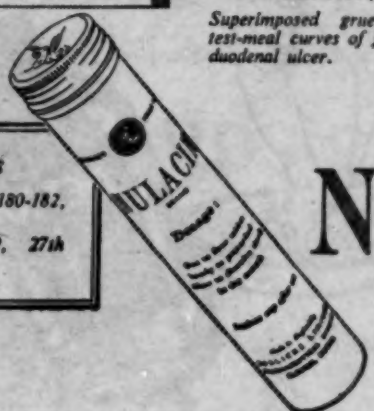

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British Medical Journal, 180-182, 26th July, 1952

Medical Press, 195-199, 27th Feb., 1952

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Journal of the
Indian Medical Association

Vol. 24, No. 5 CALCUTTA PUBLISHED TWICE A MONTH December 1, 1954

ORIGINAL ARTICLES

MYELOID METAPLASIA OF THE SPLEEN IN APLASTIC ANAEMIA

J. B. CHATTERJEA, M.D.,
Assistant Research Officer,
Indian Council of Medical Research,
AND
C. R. DAS GUPTA, M.B., D.T.M., F.N.I.,
Department of Haematology, School of Tropical Medicine, Calcutta.

The phenomenon of extramedullary haematopoiesis in a wide variety of clinical conditions associated with depression of the bone marrow has been well documented by a number of workers (Neumann, 1880 ; Donhauser, 1908 ; Erf and Herbert, 1944 ; and Heller *et al*, 1947). In conditions of widespread fibrosis and/or sclerosis of the bone marrow, spleen and sometimes the liver may undertake the function of haematopoiesis and undergo remarkable degrees of enlargement (Wyatt and Sommers, 1950 ; Block and Jacobson, 1950 ; Chatterjea *et al*, 1952).

It is conceivable that in idiopathic aplastic anaemia which in reality represents a condition of progressive bone marrow failure, the spleen may take up the embryonic function of haematopoiesis and prolong the life of the patient without blood transfusion. But the development of extramedullary haematopoiesis in a classical case of aplastic anaemia is extremely rare. We had the opportunity of studying in detail the gradual evolution of the process of myeloid metaplasia in a young man who originally presented himself as a classical case of aplastic anaemia of the idiopathic variety.

Case Report

P.P., Hindu male, aged 22 years, was admitted into the Carmichael Hospital for Tropical Diseases on 31-3-50 with complaints of progressive anaemia not responding to intensive therapy with liver extracts and iron. Until about three months prior to admission the patient was well, doing his normal duties as a salesman in a grocery of Calcutta. Onset of illness was insidious and the main symptomatology consisted of asthenia, anorexia together with palpitation and breathlessness on slight exertion. The patient had also noticed slight gum bleeding off and on. On examination significant clinical findings were marked pallor, enlargement of the liver (1 cm. below costal arch), slightly dilated heart with a weak first sound in mitral area and soft systolic murmurs without any conduction in mitral and pulmonary areas. Blood pressure was 125/60 mm. Hg. Thorough system reviews did not reveal any other abnormality. The spleen was not palpable. The patient was afebrile on admission but later on ran a low-grade intermittent fever off and on. Past history and family history were non-contributory. No history of any exposure to infections or toxic agents viz., chemicals, drugs or irradiation could be traced.

Laboratory Data :

Blood (on admission) : Haemoglobin—4·64 g., R.B.C. —1·8 million, P.C.V.—18·0 per cent, M.C.V.—100·0 cu. μ, M.C.H.—25·7 $\gamma\gamma$, M.C.H.C.—25·7 per cent, reticulocyte 0·2 per cent. Total W.B.C.—3,900, neutrophils 1,950, lymphocytes 1,755, monocytes 78, eosinophils 117 per c.mm. No abnormal nucleated cells in peripheral blood smear. Platelets 60,000 per c.mm. Total plasma protein 6·89 g., albumin 3·25 g. 2 globlin 3·64 g. Van den Bergh test—direct negative, indirect 0·2 mg. Serum iron 150 microgram. Total cholesterol

132 mg., free cholesterol 31 mg. Aldehyde test—negative; Chopra's test for kala-azar—negative; complement fixation test for kala-azar—negative. Wassermann reaction and Kahn test negative. Thymol turbidity—2·0 Mclagan units. Hippuric acid excretion 1·09 g. per hour. Bleeding and coagulation times were normal. Patient's serum did not show any demonstrable haemolysin or haemoagglutinin either in saline or albumin medium. Both direct and indirect Coombs tests were negative.

Bone marrow was extremely hypocellular with great reduction of erythropoietic, granulopoietic and thrombopoietic elements. Depressed erythropoiesis was normoblastic with preponderance of mature normoblasts. Lymphocytes and plasma cells comprised the major bulk of marrow cells. The picture in brief was one of classical aplastic anaemia. Altogether six aspiration biopsies were performed during the period between March 1950 and January 1953 and the results each time were identical. Trephine biopsy of bone marrow on 4-6-52 confirmed the aplastic condition and excluded neoplastic infiltration, fibrosis or sclerosis of the bone marrow. Photomicrographic appearance of the trephine biopsy material is shown in Fig. 1 (*vide* Plate).

Splenic puncture was done on 21-5-52. Splenic smear showed evidences of extensive myeloid metaplasia. The splenogram was grossly abnormal with depressed lymphopoiesis and greatly increased myelocytosis and normoblastosis. Fig. 2 (*vide* Plate) shows the photomicrographic appearance of splenic cytology and the details of splenogram are given in Table I.

TABLE 1—SPLENOGRAM.

Normoblast		
A	None seen	
B	Occasional	
C	40·50%	
Megaloblasts	None seen	
Total nucleated red cells ...	...	40·50%
Neutrophilic myelocyte ...	6·75%	
,, meta myelocyte	2·00	
,, band ...	14·00%	
,, segmented ...	Occasional	
Eosinophilic myelocyte band	1·25%	
,, segmented ...		
Total granular cells ...	...	24·00
Lymphocytes	30·5%	30·50%
Reticulum cells	...	2·75%
Monocytes	...	2·25%
Megakaryocytes	None seen	
Parasites	None seen	
Malarial pigments ...	None seen	

Urine—No abnormality detected.

Stool—Oxyuris ova and cysts of *Entamoeba histolytica* were found.

Fractional gastric analysis showed isochlorhydria.

Adrenaline test (Doan and Wright 1946) was done on 14-12-51 when the peripheral blood was leucoerythroblastic. There was no rise in R.B.C., haemoglobin, haematocrit and platelet levels. Total nucleated cell count, however, increased by 100 per cent. The results of the test indicated that the nucleated cells were available in the system for mobilisation in the peripheral blood. Bone marrow being aplastic, the source of these cells was obviously the extramedullary tissues. The poor erythrocytic and thrombocytic responses in all probability reflected inadequate production and storage of these cells (Chatterjea *et al*, 1953).

Skiagram of chest, skull and vertebrae did not show any abnormality. There was no evidence of osteosclerosis.

CLINICAL AND HAEMATOLOGICAL PROGRESS (Fig. 3):

Administration of ferrous sulphate tablets, vitamin C and crude liver extracts did not produce any clinical or haematological improvement. Repeated small transfusions of whole blood along with methionine, proteolysed liver extract were also of no use.

Towards the middle of May, 1950, the reticulocyte count was 0·6 per cent and the peripheral blood showed a few neutrophilic myelocytes and occasional normoblast without any increase of total W.B.C. count. Thereafter reticulocyte count varied from 0·6 to 1·5 per cent and from the middle of September 1950, peripheral blood became progressively leuco-erythroblastic with many normoblasts and myelocytes. On 20-6-50 he had an attack of benign tertian malaria which was quickly controlled by a course of quinopamaquine administered under the direction of Professor R. N. Chaudhuri. Splenic enlargement was detected for the first time on the same day (20-6-53) and subsequently there was a progressive splenomegaly. Plasma bilirubin level began to increase from 22-11-50 and subsequently reached the maximum level of 1·5 mg. per 100 ml. about 2 months later on 18-1-51. There was, however, no significant correlation between the blood picture and the plasma bilirubin level. Along with splenomegaly he had also hepatomegaly and still later about one year after admission he developed slight degree of cervical lymphadenopathy, as well. Subsequent course of the patient was characterized by:

(*i*) Progressive splenomegaly, leuco-erythroblastosis, reticulocytosis and increase of R.B.C., haemoglobin, and haematocrit values. The haematological improvement was independent of the various therapies viz., liver extract (parenteral and proteolysed), iron (oral and intravenous), folic acid, vitamin B_{12}, vitamin B complex, vitamin C, methionine, cholesterol (5 per cent solution in oil given intramuscularly in the dosage of 2 c.c. daily), cobalt chloride solution (2·5 per cent aqueous solution—4 to 6 c.c. daily by mouth—4 c.c. of the solution is equivalent to 100 mg. of cobalt), thyroid extract, A.C.T.H., penicillin, quinine and repeated transfusions of whole blood or packed red cells. Platelet count, however, did not rise and this finding would explain the bouts of gum bleeding persisting even at the height of R.B.C., haemoglobin and haematocrit levels.

(*ii*) Series of relapses. The patient's R.B.C., haemoglobin, and haematocrit levels were never steady and he had a number of relapses. A direct relationship between patient's haematologic status

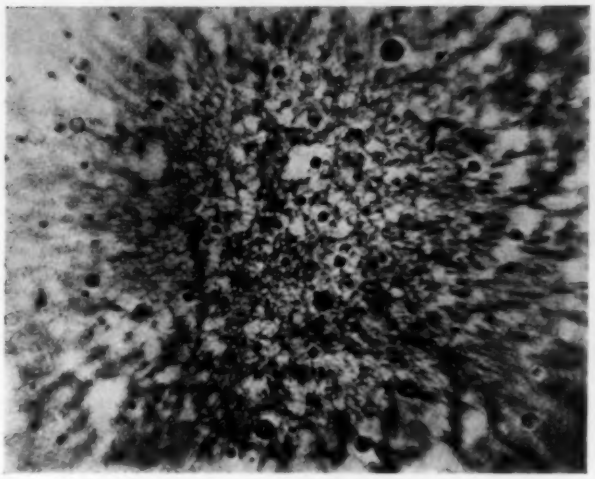


Fig. 1—Histological section of bone marrow obtained by trephine biopsy. A virtually acellular bone marrow, characteristic of aplastic anaemia. ×215.

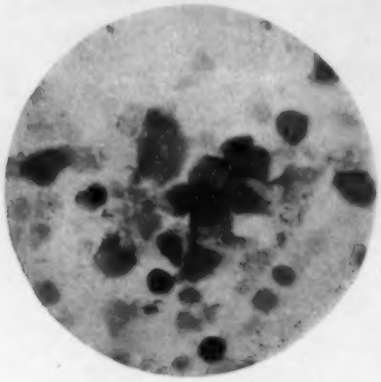


Fig. 2—Splenic smear stained with Leishman's stain. Replacement of lymphocytic cells by myelocytes and normoblasts indicates myeloid metaplasia of the spleen. ×540.

CHATTERJEA AND DAS GUPTA—*Myeloid Metaplasia of the Spleen in Aplastic Anaemia (pp. 165-68).*

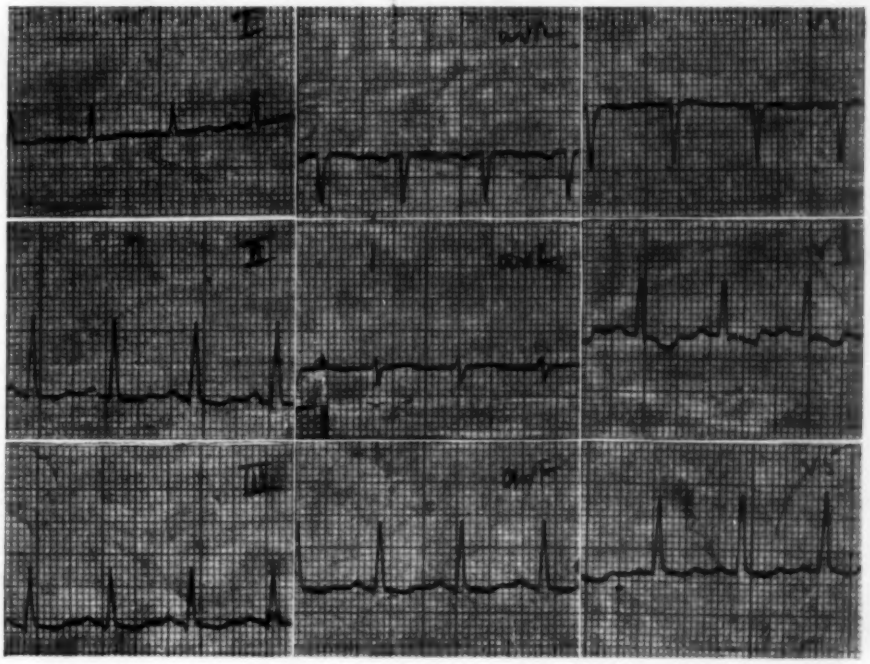


Fig. 1—Electrocardiogram showing flat and inverted T in some of the leads and depressed S-T segment in V_5.

GANGULI AND MUKHERJEE—*Addison's Disease—Report of a Case (pp. 189-90).*

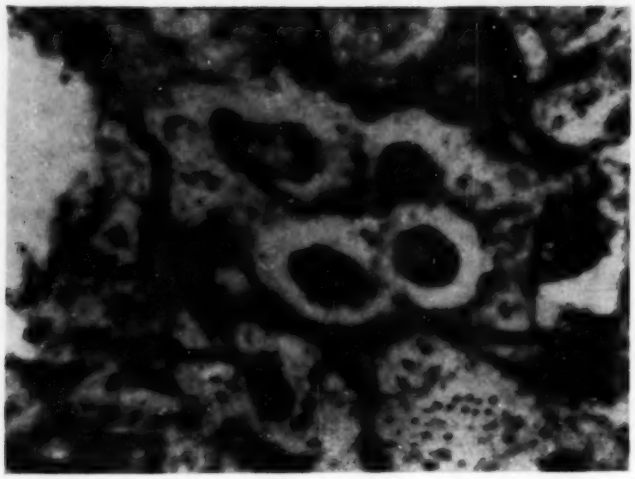
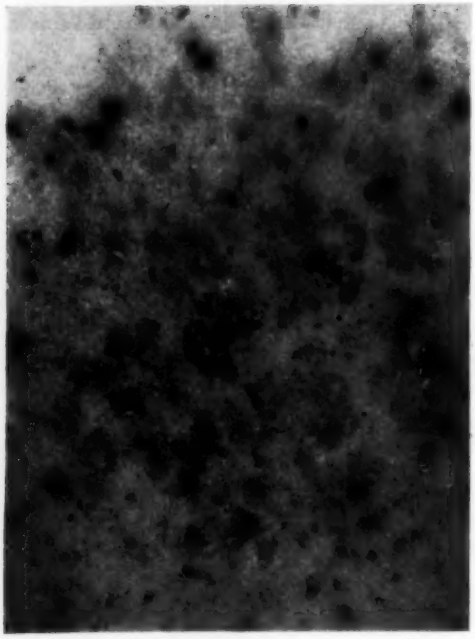
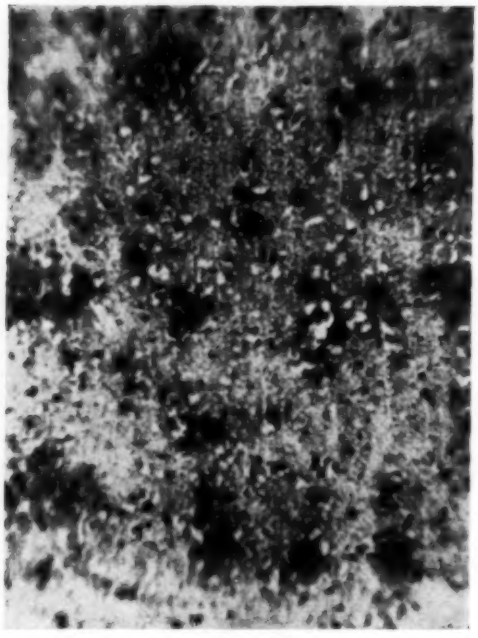


Fig. 1—Showing ' capsulated organisms ' in direct smear of the pus.





Figs. 2 and 3—' Capsulated organisms ' from culture stained by dry film Indian ink method.

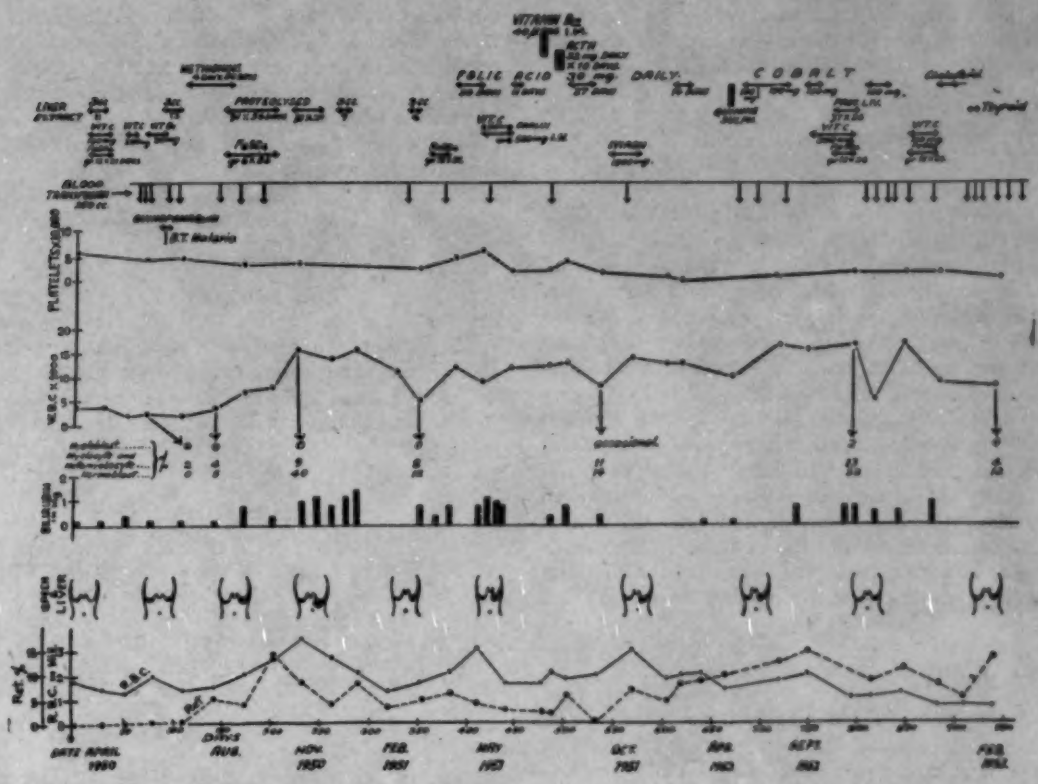


FIG. 3—GRAPHIC REPRESENTATION OF CLINICAL AND HAEMATOLOGICAL COURSE.

and the degree of splenic enlargement was observed. Greater enlargement of the spleen was usually associated with improvement of blood picture and decrease of splenic size was always associated with clinical and haematological deterioration. The patient himself noticed that he was comparatively better with a large spleen 'filling up the abdomen'.

Ultimately the spleen failed to meet the increasing haemopoietic demands arising from progressive marrow failure and the patient died on 25-2-53, 3 years after his first admission into hospital. Unfortunately autopsy permission could not be obtained.

DISCUSSION

Originally starting as an aplastic anaemia without any splenomegaly this patient gradually developed myeloid metaplasia of the spleen and also possibly of the liver and the lymph nodes. Myeloid metaplasia as a sequela to myelofibrosis and myelosclerosis is well known (Wyatt and Sommers, 1950 ; Block and Jacobson 1950 ; Chatterjea *et al*, 1952). But myeloid metaplasia occurring in a case of aplastic anaemia has not probably been reported before, though it has been suggested that myeloid metaplasia may occur whenever bone marrow is depressed. In classical aplastic anaemia there is universal aplasia of haemopoietic tissues all over the body and enlargement of the spleen, liver and lymphnodes is characteristically absent. It is presumed that whenever the noxious agent is sufficiently potent and has acted for a sufficiently long time, haemopoietic depression would be widespread affecting all the organs. If, however, the toxic agent is mild and the period of exposure short the haemopoietic depression may be selectively confined to the more vulnerable bone marrow elements. In such a situation the extramedullary tissues might retain their functional integrity and undergo myeloid metaplasia as a compensatory mechanism. Myeloid metaplasia may help to tide over the critical period of acute bone marrow depression. Experimental confirmation of such a conception is available from the irradiation experiments of Jacobson *et al* (1949). They found that survival rate of irradiated mice was higher when the spleen

was protected from irradiation injury by a proper shield. The shielded spleens of protected animals showed extensive myeloid metaplasia.

Influence of Malaria on Myeloid Metaplasia :

Splenic enlargement in this patient was first seen during a clinical attack of malaria. The question naturally arises whether malarial infection incited the whole process of myeloid metaplasia. Slight degree of myeloid metaplasia may be seen in chronic malaria and an occasional case of aplastic anaemia may follow malarial infection in a vulnerable subject. It is, however, most unlikely that malarial infection was responsible for the development of extensive myeloid metaplasia in a patient who had been aplastic to start with. The possibility that latent malarial infection at first induced aplasia of the bone marrow and later on incited haemopoietic changes in the extramedullary tissues cannot, however, be entirely dispensed with. But such a possibility must be remote.

Role of Any Haemolytic Component :

Association of splenomegaly with reticulocytosis and hyperbilirubinaemia is suggestive of the presence of a haemolytic component. These features which were absent in the beginning had however, no distinct correlation with the degree of anaemia (Fig. 3). Splenomegaly and reticulocytosis heralded the beginning of splenic haematopoiesis and was followed by clinical and haematological improvement. Hyperbilirubinaemia was probably indicative of rapid destruction of malformed splenic erythrocytes. Absence of any demonstrable agglutinins or haemolysins and negative Coombs test indicated that no immunologic mechanism was responsible for the haemolysis.

Spleen and Bone Marrow :

The exact interrelationship between the spleen and bone marrow in normal haematopoiesis is uncertain. Normal spleen is said to maintain an equilibrated blood picture either through a direct sequestration-phagocytosis mechanism (Doan and Wright, 1946) or through an inhibitory influence on the bone marrow controlling the maturation and delivery of formed elements (Dameshek, 1944 ; Dameshek and Estren, 1947). On the basis of such an idea splenectomy has been carried out in aplastic anaemia with a view to remove the inhibitory influence ("Splenism") on the marrow. An expansion of this idea may be seen in the term "hypersplenism" which embraces all splenomegalic pancytopenias curable by splenectomy. The clinical finding of extensive splenic myeloid metaplasia in conditions of chronic bone marrow failure as also the experimental works of Jacobson *et al* (1949) tend to argue strongly against the validity of splenectomy in aplastic conditions ; more so when there is associated myeloid metaplasia of extensive degree.

Summary

Evolution, progress and termination of myeloid metaplasia supervening in a young adult male with idiopathic aplastic anaemia is described in detail. Implications of the pathogenetic process are discussed.

Acknowledgment

Our thanks are due to Dr. P. Chatterjee, formerly Professor of Surgery, Medical College, Calcutta, for the trephine biopsy of bone marrow; to Dr. P. C. Sen Gupta for the histological examination of bone marrow; and to Dr. P. Basu for liver function tests.

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STUDIES ON THE PHARMACOLOGY AND CHEMOTHERAPY OF A DIHYDRO-TRIAZINE DERIVATIVE*

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AND

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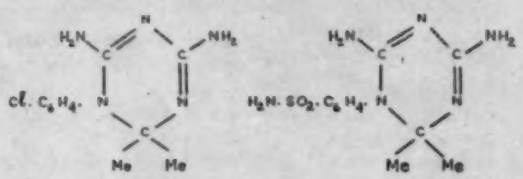
The common human malaria parasites, *P. falciparum* and *P. vivax* are susceptible to sulphonamides (*cf.* Coggeshal *et al*, 1941) and therefore they presumably need p-aminobenzoate as a growth factor. The observations of Greenberg and his collaborators (1948) and of Greenberg (1949) again tend to establish that the antimalarial activity of proguanil is activated by sulfa drug. But the activity of the above antimalarial is being found (*cf.* Carrington *et al*, 1951 and Crowther and Levy, 1953) to be due to some metabolic breakdown product of the dihydrotriazine type (I). It was naturally considered to be of importance to study the antimalarial characteristics of a compound (II)—a sulfa-triazine derivative synthesised (Basu *et al*, 1952) in this laboratory in another connection. Chemically the compound is 2 : 4-diamino-1-p-sulphonamidophenyl - 1 : 6-dihydro-6 : 6-dimethyl-1 : 3 : 5-triazine (II) and its similarity with the triazine (I) isolated as the metabolic product from proguanil would be evident from the structural representation as shown below :



(I) (II)

The systematic investigation including chemical evaluation have accordingly been carried out and the results, thereof, are being incorporated in this paper.

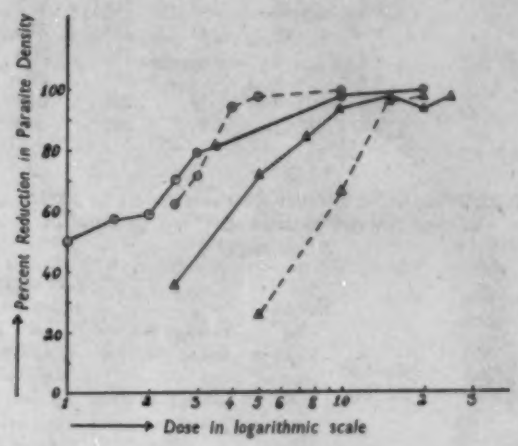
METHODS AND MATERIALS

ANTIMALARIAL ACTIVITY :

The sulphodihydrotriazine derivative (II) was tested against two malarial strains, *P. gallinaceum* in one-week old leg horn chicks, and *P. berghei* in in-bred white mice of weight 20-21 g. The inoculum in chicks consisted of 40-50 million infected red blood corpuscles in 1 per cent citrated saline, given intravenously. Mice were inoculated with 1 million infected red blood cells per g. of body weight, intraperitoneally. By such inoculation, the peak parasitaemia in both species of animals was reached on the 5th day.

Blood from all the inoculated animals was examined on the 5th day of inoculation (the day following the last dose of the drug) by taking both thin and thick smears. The density of parasitaemia was noted by recording the number of infected red blood cells out of a total count of 1000 cells. The criterion of antimalarial activity was determined by noting the percentage reduction of parasite density in treated animals, in comparison with that of the control groups without treatment.

The drug was fed as an emulsion in gradually increasing doses to groups of inoculated animals keeping a group as untreated control for each dose. Each dose was administered once on the day of inoculation and repeated twice daily for the following three days. A dose response curve was drawn on a logarithmic scale, and the effective dose level (M.E.D.) on the basis of a 75 per cent reduction in parasite density, was calculated by interpolation (Fig. 1).



P. berghei: Sulpho-dihydrotriazine derivative
Quinine

P. gallinaclum: Sulpho-dihydrotriazine derivative
Quinine

FIG. 1

Parallel experiments with quinine were also carried out, and the response plotted on the curve. The quinine-equivalent (Q.E.) of the dihydrotriazine (II) based on the ratio of M.E.D. of quinine/ M.E.D. of compound (II) was thereby determined (*cf.*, Wiselogle, 1946). It was found that the Q.E.

* Supazine.

was 2·0 Q against *P. berghei* infection, and 3·5 Q against *P. gallinaceum* infection.

TABLE 1—SHOWING DENSITY OF PARASITAEMIA AS EFFECTED BY THE DIHYDROTRIAZINE (II) AND QUININE IN *P. berghei*.

Drug.	Dose in mg/20g.	Number of animals in treated or control group	Average 5th day parasitised cell count per 1000		Per cent reduction of parasite density by drug compared to control
			Treated group	Control group	
Dihydrotriazine (II)	0·1	5	120	240	50
	0·15	5	102	240	57·5
	0·2	5	100	240	58·4
	0·25	10	72	240	70
	0·3	10	42	200	79
	0·4	10	38	200	81
	0·5	10	20	200	90
	1·0	5	6	200	97
	2·0	5	3	282	99
Quinine	0·25	5	155	240	35·4
	0·5	10	68	240	71·7
	0·75	10	41	240	83·0
	1·0	5	12	183	93·4
	1·5	5	7	300	97·7
	2·0	5	16	220	92·7
	2·5	5	10	290	96·6

TABLE 2—SHOWING DENSITY OF PARASITAEMIA AS EFFECTED BY THE DIHYDROTRIAZINE (II) AND QUININE IN *P. gallinaceum*.

Drug	Dose in mg/50g.	Number of chicks in treated or control group	Average 5th day count per 1000		Per cent reduction of parasite density by drug compared to control
			Treated group	Untreated group	
Dihydrotriazine (II)	0·25	3	250	660	62·2
	0·3	3	192	660	71·0
	0·4	3	38	660	94·3
	0·5	3	18	620	97·2
	1·0	3	10	620	98·4
Quinine	0·5	3	455	620	26·6
	1·0	3	206	620	66·7
	1·5	3	23	620	96·3
	2	3	21	620	96·7
	2·5	3	20	620	96·8

TOXICOLOGICAL STUDY:

On Mice—Acute oral and intraperitoneal toxicity of sulfa-dihydrotriazine were carried on white mice, mortality being observed up to a period of one week. It was found that a dose of 75 mg. per 20 g. body weight of mouse was the highest tolerated dose for a single administration. The intraperitoneal LD 50 calculated from a log-dose mortality curve was found to be 3·31 mg. per 20 g. or 0·1655 mg. per g. (Fig. 1, Tables 3 and 4).

TABLE 3—SHOWING ACUTE TOXICITY AFTER SINGLE ORAL ADMINISTRATION (WT. OF MICE 20-22 g.)

Dose Quantity of drug 20 g.	Number of mice used	Number of mice surviving on days							Final mortality	Highest tolerated dose mg./g.
		1	2	3	4	5	6	7		
5 mg.	5	5	5	5	5	5	5	5	0/5	
12·5 mg.	5	5	5	5	5	5	5	5	0/5	
25 mg.	3	3	3	3	3	3	3	3	0/3	
35·5 mg.	5	5	5	5	5	5	5	5	0/5	3·75
50 mg.	6	6	6	6	6	6	6	6	0/6	
75 mg.	3	3	3	3	3	3	3	3	0/3	
100 mg.	3	2	1	1	1	1	0	0	3/3	

TABLE 4—SHOWING ACUTE INTRAPERITONEAL TOXICITY (WT. OF MICE 20-25 g.)

Dose/20 g.	Number of animals used	Number of mice dying in 7 days	LD50 mg./g.
37·5 mg.	5	5/5	
25·5 mg.	5	5/5	
12·5 mg.	5	5/5	
10·0 mg.	5	3/5	0·1655
9·6 mg.	5	5/5	
7·5 mg.	5	5/5	
5·0 mg.	5	5/5	
3·6 mg.	5	3/5	
2·4 mg.	5	1/5	

For chronic toxicity test, groups of mice were fed with different doses of the drug for a period of two weeks and the animals observed for 7 weeks. A control group was also kept. It was found that a dose of 5 mg. per 20 g. for two weeks was well tolerated by the animals, without any untoward effect. A dose of 12·5 mg. per 20 g. caused a low percentage mortality 6·6 per cent and is probably very near to the highest tolerated dose.

TABLE 5—SHOWING CHRONIC TOXICITY (AFTER DAILY FEEDING OF DRUGS FOR TWO WEEKS IN MICE WEIGHING 20-22 g.)

Dose mg. per 20 g.	Number of animals used	Number of mice surviving after week						Final mortality
		1st.	2nd.	3rd.	4th.	5th.	6th.	
25·0	10	9	8	...	...	...	8	2/10
12·5	10	9	7	7	7	7	7	3/10
12·5	15	15	14	14	14	...	14	1/15
5·0	5	5	5	5	5	...	5	0/5

Thus it can be taken that the mice tolerated about 40 times or more the M.E.D. required to abort a malarial infection.

On Rabbits—The effect on growth and haematological changes, brought about by the administration of the drug for a continued period of 3 months was studied on young rabbits, in comparison with a group of control animals. The data are recorded in Tables 6 and 7.

It can be seen, that with continued feeding of the drug for 12 weeks the treated animals had even a greater gain in total weight than that of the corresponding controls. Their findings may or may not be significant. But intestinal antisepsis, caused by the feeding of a sulphonamidotriazine compound may have some biological effect reflected in better assimilation of food.

There was no marked change in the haematological data during the period of first 8 weeks. Thereafter, a slight fall in the neutrophil percentage was noticeable, which was quickly overcome by discontinuation of the drug. There was no marked change in the haemoglobin level.

HAEMOLYTIC ACTION AND METHAEMOGLOBIN FORMATION:

Comparative tests were put up *in vitro* with mixtures of washed human red blood corpuscles, suspended in 0·85 per cent, saline and different amounts of dihydrotriazine or quinine. Even in as high a concentration as 1 per cent, the triazine derivative showed no haemolytic action, while quinine caused a total haemolysis of red cells. No band of methaemoglobin formation could be detected with the spectroscope, even after contact of the drug with oxalated blood from 3 hours.

TABLE 6—SHOWING WEIGHT VARIATION IN RABBIT AFTER CONTINUOUS DAILY ORAL ADMINISTRATION OF THE EFFECTIVE DOSE (60 mg./kg.) FOR A PERIOD OF 12 WEEKS

		Original wt. in g.	Week 1st.	2nd.	3rd.	4th.	5th.	6th.	7th.	8th.	9th.	10th.	11th.	12th.	Total gain or loss
Treated	1	1330	+10	+50	+10	+30	+20	±	±	+30	+20	±	+20	−10	+180
	2	900	+30	−20	+40	+70	+50	+30	+20	+20	+60	+40	+100	+40	+480
	3	1070	+30	+20	±	+40	+20	+20	−20	−10	−20	+30	±	±	+110
	4	1350	±	+20	−70	+20	−20	+90	−10	±	+70	+100	+50	−50	+200
Control	1	1300	−80	+60	−100	+120	−30	−40	−30	+50	−30	±2	+10	+20	−50
	2	1230	−30	±	+20	+70	−70	+20	+110	−50	−20	−10	±	±	+40
	3	1100	−90	+10	+30	+70	±	±	−70	+20	+80	−30	+80	−10	+90
	4	1320	+20	+30	+20	+90	−30	−50	−30	±	±	−80	−10	+40	±

TABLE 7—SHOWING HAEMATOLOGICAL CHANGES

(AVERAGE OF FOUR RABBITS BEFORE, DURING AND AFTER DISCONTINUATION OF THE DRUG. THE DRUG WAS GIVEN IN 6 TIMES THE EFFECTIVE DOSE ONCE DAILY FOR 12 WEEKS)

	Average r.b.c. in million	Average w.b.c. in thousand	Average neutrophil %	Average lymphocyte %	Average monocyte %	Average eosinophil %	Average Hb. %
Before drug administration ...	5·6	13·1	55	40	3	2	80
At the end of 4th week of drug treatment	5·4	13·0	50	42	5	3	75
At the end of the 8th week ...	5·0	11·5	45	50	3	2	80
At the end of the 12th week ...	4·9	9·0	40	53	3	4	80
Ten days after discontinuation ...	5·0	11·0	46	50	2	2	90

EFFECT ON HUMAN MALARIA :

In view of the low toxicity of the compound (II) and its powerful antimalarial activity in experimental animals, it was considered worthy of trial in the clinical field. Accordingly, a number of cases of human malaria were taken up for the study. Some patients had the treatment during the primary attack, while others had it during an acute attack following several relapses. A total of 20 cases were studied of which 3 were children within the age of 5 years and the rest adults. 25 per cent of the cases were females. Of the 20 cases, 2 had infection with malignant tertian parasite, 1 had quartan, 1 was clinically diagnosed without blood examination, and the rest were all cases of benign tertian infection. 50 per cent of the cases were of the relapsing type, and had previous treatment with various other antimalarials such as quinine, paludrine or mepacrine.

After a thorough physical and blood examination each adult patient was fed with 1 g. of the drug daily, divided into two doses. The total dose required to cure a clinical attack was found to vary between 3-4 g.; the parasites disappeared from the peripheral blood within 24-36 hours ; the period of therapy lay between 4-6 days. The children were given doses in proportion to age. After the control of the fever a weekly dose of 0·25-0·5 g. for 1 to 3 weeks was given to 11 patients. 4 patients showed one or two relapses, which were again treated with the triazine derivative. No relapse, in any case has been reported thereafter till the time of report (1-1½ years). There was no complaint of any untoward reaction during the administration of the drug.

DISCUSSION

Inspite of the introduction of several antimalarials, the problem of prophylaxis and cure of relapsing malaria, still defies proper solution. The drawbacks of proved remedies, such as quinine, plasmochin, mepacrine and similar compounds led to investigations on an extensive scale in America and other places, during the last World war when more than 16,000 compounds were tested experimentally. Researches are however still being pursued (*cf.* Basu *et al*, 1950 ; Chandran *et al*, 1952) to find out more powerful remedies. Proguanil when first introduced appeared to show a great promise. But, on account of the emergence of quick drug resistance of parasites (Bishop and Birkett, 1947 ; Editorial, *B.M.J.*, 1949) its use in clinical medicine has become restricted. Other compounds (*e.g.* pyrimethamine) showing very high quinine equivalent activity against *P. berghei*, and *P. gallinaceum* (Falco *et al*, 1951) have not been able to keep parallel corelation in activity on human malarial strains (Chakravarti and Chaudhuri, 1953 ; Robertson *et al*, 1952). These findings show that clinical evaluation is still the sheet anchor for the establishment of any antimalarial, however, more potent than quinine or other known drug it may be in experimental infection.

Considering these paints, it seems rational to follow up the trial of the new dihydrotriazine on a field scale on human malarias of different races and countries. It has got powerful suppressive action, acting mainly on the asexual forms of the parasites of human malaria. Its quinine equivalent in experimental animal showed sufficient promise, which could be verified in the small number of human malaria cases. Its oral toxicity was unusually low. Prolonged administration rather had a beneficial effect on the general health. Being free from any haemolytic action, the compound could be safely administered even in cases of black water fever, where quinine would be contraindicated. The total dose required for tackling a clinical attack was much less than quinine, and the cost of treatment was also very low.

The intraperitoneal toxicity of the compound however showed a higher figure than that of the oral tolerated dose (Table 4). The low slope of the dose response curve points to a log in the attainment of quick response with increase in dose (Fig. 1). Correlating this finding with the high intraperitoneal toxicity, it seems that the compound is either slowly absorbed in the system, or that during passage through the organs such as liver, it is changed to some other product. Work on the absorption, blood concentration and metabolic changes associated with its circulation and excretion, will be worthcarrying, and all these investigations are in progress.

ACKNOWLEDGMENT

The drug used in the clinical investigation is the hydrochloride of the compound II kindly supplied by Messrs. Bengal Immunity Co., Ltd. in the form of Supazine tablets each 0·25 mg.

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VOLVULUS OF THE SMALL INTESTINE

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Volvulus of the small intestine is a type of intestinal obstruction that is rarely mentioned in literature. Wilson (1949) was able to collect records of only 61 reported cases of volvulus of the small intestine. Most of these cases are from the African tribes. However, the condition appears to be not so rare in certain parts of India—Western U.P., Bihar, Assam and Rajasthan. Mc Watters recorded 12 cases from Western U.P. during 1919-32. Perhaps the most outstanding contribution on this subject, especially on its pathology, seems to be from India. Banerji (1950) reported and reviewed over 300 personal cases, easily the largest series of cases so far reported. The present paper is based on 15 such cases in a series of 75 cases of acute intestinal obstruction in Nalgonda and Warangal Districts of Hyderabad State where the condition is fairly common.

INCIDENCE

During the period of from 1950 to 1953 (July) the total number of acute intestinal obstruction cases surgically treated was 75.

1.	Strangulated hernia ...	32
2.	Volvulus of sigmoid ...	6
3.	Volvulus of caecum ...	4
4.	Volvulus of small gut ...	15
5.	Bands including Meckel's ...	5
6.	Ileocaecal intussusception ...	1
7.	Chylocele of mesentery ...	1
8.	Malignant growths ...	2
9.	Imperforate anus	9

Thus small intestinal volvulus forms 20 per cent of all acute intestinal obstructions and 60 per cent of all volvulus cases. This may be compared with other figures in literature (Table I).

TABLE I.

Name of author and year	No. of cases of acute obstruction	No. of cases of small intestine volvulus
Banerji (1950) ...	... 603	300 (50%)
Ojah (1950) ...	... 110	18 (18%)
Kerr and Kirkaldy-Wills (1946)	21	7 (33%)

All the cases in this series are male adults and belong to the labouring class. There is no particular seasonal incidence. The staple diet of these patients is mostly jowar.

AETIOLOGY

Volvulus of the small intestine can be classified on an aetiological basis as follows:

1. Volvulus due to errors of rotation of gut, including volvulus neonatorum.
2. Volvulus due to bands, including Meckel's diverticulum usually involving the whole or isolated loop or loops.
3. Idiopathic group involving the whole length of the small gut.

The present series of cases belong to the third group. The exact aetiological factor is not known. Banerji (*loc. cit.*) has summarised his views on aetiology as follows:

1. The fact that the situation of the twist is almost always at the superior mesenteric vessels suggests the persistence of the tendency towards rotation, as inherent unstable equilibrium, as a possible factor.
2. The fact that it is in "heavy eaters" indicate a dietetic factor.
3. Co-existing bowel infection is so common in these cases that it may have an aetiological importance.
4. The sex incidence in favour of males suggests that the muscular anterior abdominal wall of the male prevents spontaneous restitution easily while in the female the lax adbominal wall permits this with ease.

It is said that a coarse diet of millet or jowar is an aetiological factor. In coastal Andhra Districts where the staple diet is rice the condition is extremely rare. Habitual eaters of heavy diet is said to have an elongated mesentery, specially the ileal part where food stagnates. This elongation of the

mesentery predisposes to volvulus. A heavy meal on an empty stomach or after a period of starvation or heavy manual labour after a full meal sometimes seems to be the immediate cause of an attack. Two cases in this series got the attacks while working on the fields after the morning meal of jowar. Over-eating during festivals is another possible immediate cause. Pathological changes in the mesentery due to conditions like tuberculosis of lymph glands which alter the mobility and texture, may also predispose to volvulus but not met with in this series.

Ogilvie (1946) observes, "South African anatomists have told me that the African small intestine is usually several feet longer than that of the European and Vint also believes this to be the case. The appendix is longer and the stomach larger but not otherwise different. The mesentery is either longer or more extensile, for at laparotomy or necropsy the intestine can be lifted more easily to the surface for examination or manipulation, anomalies of intestinal rotation and fixation are much more common, particularly the persistence of unfixed mesenteries. It is possible that it is in this greater mobility of the mesentery of the alimentary canal rather than in his dietary habits that the reason for that proneness of the African to volvulus is to be found".

The clinical picture in these cases is one of typical low small intestinal obstruction but the operative findings are so curious that one is likely to miss the condition unless he is aware of it. On opening the abdomen distended loops of small intestine present themselves into the wound and on exploration the caecum will be found not in the right iliac fossa but lifted upwards and to the left. The caecum is collapsed. Even a careful search may not reveal any obvious obstructing element and the surgeon may even proceed to close the abdomen thinking that he has performed an unnecessary laparotomy. Rowlands and Turner (1937) have stated "in several cases difficulties were so great and the appearance so puzzling that the operators did not recognise the condition during the operation." But for one who is in the know of the exact pathology, the diagnosis is obvious.

The basic mechanism of the volvulus of the small intestine is not the same as that of the sigmoid. The mesentery of the sigmoid has a narrow parietal attachment and can rotate on itself a number of times. On the other hand, the mesentery of the small intestine has a wide parietal attachment and fans out to accommodate the entire length of the gut. It cannot rotate on itself even one complete turn. What exactly happens is, that part of the mesentery belonging to the lower ileum gets doubled up over the rest of the mesentery. This folding up of the mesentery, invariably takes place at the site of the superior mesenteric vessels and is clock-wise in direction. The caecum is lifted up and to the left and the posterior surface of the mesentery becomes the presenting surface. The terminal ileum also gets altered in its position. Instead of running downwards and outwards to meet the caecum, it now runs upwards to meet the lifted up caecum. It now seems to emerge from beneath the folded up mesentery and the site of obstruction is where it so emerges. The alteration in the disposition of the caecum and the terminal ileum and the presence of the tense border of the folded mesentery are most significant and diagnostic operative features.

It is most likely that such folding of the mesentery on itself is a normal occurrence during the physiological peristaltic activity of the small intestine and undergoes spontaneous restitution. But due to some reason when the restitution fails to occur, the puzzling condition of the volvulus of the small intestine results. It is not in fact so much a volvulus as an exaggerated kinking or folding of the mesentery. In the early stages the constricting element namely the border of the folded mesentery is lax and smooth and the obstruction is therefore incomplete. In the words of Salisbury Wood (1945) "the affected loops swing like a ship at anchor, partially folding over and then swinging free again with temporary remissions of symptoms" until the increasing distension and weight of the affected loops render such a process impossible.

Volvulus of the small intestine is not a loop obstruction like that of the sigmoid. It is only an obstruction in continuity, the constricting element being the folded border of the mesentery which presses upon the terminal ileum. In late cases the sites of obstruction are well seen and left alone get necrotic and rupture. The root of the mesentery if examined carefully, shows in every case haemorrhages and oedema. Very often similar haemorrhages may be found on the anti-mesenteric border of the affected loops also as black thick patches.

Clinical Features

The clinical features are typical of low small intestinal obstruction. The onset is sudden with severe colic and initial vomit. But it is more or less subacute for a considerable time so that the general condition of the patient remains surprisingly satisfactory even in cases of four or five days duration. After the initial vomit, only in late stages does vomiting recur.

Treatment

After adequate pre-operative preparation with particular care towards fluid balance and aspiration of stomach contents, laparotomy is to be performed. The diagnosis is confirmed by the feeling of the displaced caecum which is collapsed and the ileum emerging out beneath the folded border of the mesentery.

Having established the diagnosis, the next step is to untwist the mesentery. This can be done without eventration of the gut but it appears to be wise not to attempt it for two reasons. Firstly due to the excessive distension of the loops which contain little gas and much fluid and so feel very heavy and also due to the complicated nature of the twist, the chances of such a procedure to succeed is not much and after wasting much time and shocking the patient by persisting in this step, one has to take ultimately to eventration. According to the usual teaching eventration of whole small intestine is admittedly shock producing and so is to be avoided. And the surgeon working in a cramped space filled up with distended and heavy loops of gut each most assiduously trying to slip past the retaining fingers of the surgeon and his assistant, loop after loop is delivered out for exploration and tried to be returned into the over-full peritoneal cavity. Such a classical procedure is not only shock-producing but also most unconvincing in these cases where the clinical picture is so typical and the operative findings so minimal. The surgeon, at least the occasional surgeon, feels the need for a complete exploration of the abdomen lest he should overlook some obscure condition. The second reason to take to eventration straight away is therefore to convince oneself that the diagnosis is correct and the normal anatomy is restored without any doubt.

The best procedure under these circumstances is to enlarge the incision to a sufficient length and then rapidly deliver the whole small intestine out of the peritoneal cavity and then systematically return loop after loop starting from the duodenojejunal flexure to the ileocaecal junction. This procedure automatically corrects the twist and also gives the surgeon an excellent opportunity to rapidly inspect the root of the mesentery, the large gut and other viscera. The surgeon feels sure that nothing is overlooked. The whole manoeuvre can be completed in a few minutes and is not particularly shock producing, provided the assistant keeps the loops covered and supported by a wet warm towel to prevent them from sliding down the flanks of the patient and thus put the root of the mesentery under tension. It is to be noted that it is not so much the mere eventration as the prolonged and unrestrained pull on the sensitive mesenteric root that is responsible for shock production.

In no case was it found necessary to evacuate the contents of the distended loops by an ileostomy. Further, such a procedure will not succeed any more than the expulsion of the contents of one or two loops only. With patience and gentle manipulation, it is possible to restore all the loops to the peritoneal cavity and close the abdomen in layers. Often this step in the operation is not only most trying and discouraging, but also the most shock-producing.

Once the twist is undone, the colour of the gut improves and in several cases the patient may even oblige the surgeon by passing a large stool on the table. Postoperatively paralytic ileus was not a problem. On the other hand everyone of the patients developed a mild diarrhoea on the second or third day which responded rapidly to kaolin-bismuth powders. Even repeated examination of these diarrhoeic stools did not reveal anything particular.

Results

All the fifteen cases were operated upon and except for three of them, under local anaesthesia. No case came before the third day after the onset. No case presented during the operation nonviable gut or gangrene. Four cases died, three of them within two days and the fourth after two weeks due to lung complications.

Summary

1. Volvulus of small intestine is common in certain parts of India. It is the commonest type of volvulus of gut. 15 cases of a small intestinal volvulus are presented from Nalgonda and Warangal Districts of Hyderabad State.

2. Certain aspects of its aetiology, pathology and operative treatment are discussed in detail.

3. Advantages of early recourse to eventration for correction of the volvulus are stressed.

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ON THE ELECTROCARDIOGRAPHIC TRACINGS OF A FEW AVIAN TYPES

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While working out the detailed anatomy and conducting system of the hearts of *Passer domesticus*, *Gallus domesticus* and *Columba livia* it was also desired to record their electrocardiographs for comparison with the normal human tracings. Special metallic silver electrodes were devised for the animals and every care was taken to record the tracings. The animals were of normal build and nutrition.

The observations made are recorded in a tabular form as under :

Name of the species	Rhythm	Voltage	Rate per minute
Passer domesticus ...	Regular	Normal	900
Gallus domesticus ...	Regular	Normal	375
Columba livia ...	Regular	Normal	308

PATTERN OF THE WAVES

(*i*) *Passer domesticus* :

P—Independent; QRS—0·04 sec. (duration); QT—Not discernible.

(*ii*) *Gallus domesticus* :

P—Small ; P-R—Less than 0·04 sec. ; QRS—0·08 sec. ; QT—0·14 sec. ; T—Prominent.

(*iii*) *Columba livia* :

P—Upright ; P-R—0·08 sec. ; QRS—0·09 sec. ; QT—0·16 sec.

From the above observations it is evident that heart rate in these types is exceptionally, high in comparison to other vertebrates, specially, the mammals. It is due to highly evolved and well developed conducting tissue. In addition to the usual constituents of the conducting system in higher vertebrates, i.e., sino-atrial node, A-V node, A-V bundle with its branches, the atrioventricular connections are further strengthened in these cases by the presence of additional atrioventricular muscular connections. These additional A-V muscular connections serve as additional pathways to conduct the cardiac impulse more quickly from the atria to the ventricles than has hitherto been observed in any other vertebrate type. Recently Kist (1949) has attached much importance to these accessory muscular pathways by reporting them in abnormal human heart in the event of Wolff-Parkinson-White syndrome. According to him the functional presence of these fibres cause pre-excitation of the ventricles resulting in the unusual high rate of vertebrate beats.

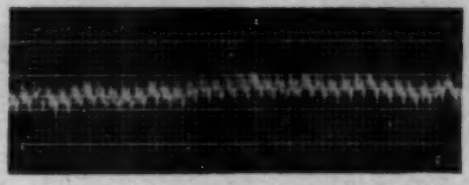

FIG. 1—ELECTROCARDIOGRAM OF *Passer domesticus* (Lead II).

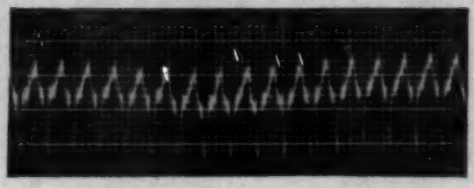

FIG. 2—ELECTROCARDIOGRAM OF *Gallus domesticus* (Lead II).

The ECG's of *Passer domesticus* indicate that P waves occur independent of QRS complex and vary in their location and contour. Sometimes they cannot be seen. It indicates the presence of ectopic centre beside the sino-auricular node. While studying the detail anatomy of the heart of *Passer domesticus* the author has recognised a distinct mass of neuromuscular tissue 'pulmonary node' at the junction of pulmonary vein draining into the left atrium. The pulmonary node is a mass of neuromuscular tissue, distinctly marked off from the rest of the atrial fibres. The position and structure of the 'pulmonary node' in the heart *Pycnonotus* definitely bears some significance on the conduction of the cardiac impulse in the atrial region.

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REFRESHER COURSE

THE DIFFERENTIAL DIAGNOSIS OF THE ANAEMIAS

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To cover this vast subject, a few guide-posts, along the road to diagnosis, may be placed to assist in arriving at a correct conclusion. Anaemia should not be considered to be definitely present unless the haemoglobin is under 70 per cent (10 g.). All too frequently a patient is found to be anaemic by a low haemoglobin, or perhaps the diagnosis is made simply by examining his mucosa, and liver therapy is unfortunately instigated without further ado. It is within the power of every conscientious physician to arrive at a fairly accurate diagnosis of what kind of anaemia he is encountering by simple inexpensive tests, and with such knowledge prescribe the specific therapy needed.

In the analysis of anaemias the following procedures are suggested, although not all may be necessary: haemoglobin, red cell count, blood smear, colour index, icteric index, haematocrit, reticulocyte count, red cell fragility test, erythrocyte sedimentation rate, mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC) and bone marrow examination. As a laboratory finding is no more reliable than the accuracy of the technician, questionable findings should be repeated. The technique of these methods is omitted.

Anaemias may be roughly grouped into three main categories both aetiologically and morphologically—those due to blood loss, increased destruction and impaired formation. To determine into which of these the presenting anaemia belongs is the first duty of the clinician. It should be emphasised here, and later, that with the exception of pernicious anaemia, a disease which seems to be very rare in India, all anaemias are secondary to some underlying aetiology. The physician, therefore, should not only diagnose the anaemia, but also find and treat its cause, otherwise he is simply treating his patient symptomatically. This, of course, requires a complete history and physical examination.

A. Anaemias due to Haemorrhage (Blood Loss)

1. *Acute haemorrhage*—The sudden loss of 1500 c.c., or even 1000 c.c., may prove fatal due to cerebral anaemia, when there is inadequate time for compensatory mechanisms to operate. Massive haemorrhage reduces the blood volume and pressure resulting in shock. If death does not supervene, vasoconstriction tries to make up for the lost volume and maintain blood pressure. Shortly, extravascular fluid enters the blood stream replacing the lost bulk, but diluting the blood so that the haemoglobin and haematocrit are lowered. After about 48 hours reticulocytes appear, and without further loss the haemoglobin is gradually restored. Acute blood loss is usually due to massive bleeding in typhoid haemorrhage, oesophageal varices, peptic ulcer, postpartum haemorrhage, or from trauma. Purpura and haemophilia may cause such a loss subcutaneously. Internal haemorrhage may be unrecognised before the signs of shock appear.

2. *Chronic haemorrhage*—Normally the bone marrow replaces daily about 1 per cent of the total red cells destroyed through wear and tear. When there is a slow loss of blood the marrow may meet this simply by throwing out more reticulocytes. An increased percentage is the only haematological evidence of bleeding as the haemoglobin remains normal. However, as bleeding goes on the bone marrow may become fatigued and the reticulocyte count falls with a consequent drop in haemoglobin. If chronic blood loss is more brisk, the increased output of new cells may not keep pace with the cells lost, and a low haemoglobin develop in spite of a high reticulocyte counts. The red cells in chronic haemorrhage are morphologically normal. The common causes of chronic bleeding are: hookworm infestation, menorrhagia, bleeding piles, slow bleeding peptic ulcers, repeated haemoptyses, etc. If other diseases or malnutrition are co-existent anaemia is naturally worsened.

B. Haemolytic Anaemias (Blood Destruction)

In this group there occurs an abnormal increase in red cell destruction within the vascular tree as a result of an intrinsic hereditary defect of the red cell itself, or a toxic action of extrinsic acquired aetiology. This form of anaemia is comparatively rare, but more and more new drugs are revealing a haemolysing effect in certain individuals, so the disease is not as rare as formerly. Very often the cause is quite obscure. The condition is characterised by periods of relapse and remission when there may be no signs of anaemia or abnormal erythrocytes, although the red cell fragility is still elevated, especially in the congenital varieties. A positive Coomb's test is often found during remission.

1. *Hereditary haemolytic anaemia* is predisposed by an inherent intrinsic defect in the erythron. Although there are a number of varieties,

it is quite rare. Congenital haemolytic jaundice of childhood and young adulthood is a disease of relapses following infection, exposure, or trauma when a high percentage of the total red cells are suddenly haemolysed resulting in a clinical "crisis" with fever, pain and prostration. Examination of the blood reveals many reticulocytes and even nucleated red cells, and small deep staining spherocytes. Poikilocytosis and anisocytosis are present. Red cell fragility is increased with complete haemolysis at 0·75 per cent saline. At the time of relapse the icterus index is high and the urine contains large amounts of urobilinogen. Any potential inciting cause must be avoided, and splenectomy usually results in remission but does not affect the underlying defect.

Other congenital haemolytic anaemias are sickle cell anaemia confined largely to negroes and thalassemia (Cooley's, or Mediterranean anaemia) both of which are probably present in India but are presumably infrequently encountered.

2. *Acquired haemolytic anaemias*—(a) Acute haemolytic anaemia of Lederer is of unknown aetiology and attacks in the first few decades. It follows a fulminant course with fever, thromboses and often fatty degeneration of the liver. Coma and uremia may precede death. Fragility and Coomb's tests are usually positive. All types of early red cells and abnormal forms of erythrocytes appear, as well as spherocytes. Transfusions may be temporarily beneficial.

(b) Chronic haemolytic anaemia is subject to remissions and relapses over a long period of years. The cause is unknown, but frequent transfusions may sensitize the patient's cells preparing the way for haemolysis. A blood smear shows normocytes, macrocytes, spherocytes and increased reticulocytes. During a relapse the icterus index as well as urinary urobilinogen is increased. The Coomb's test is positive.

(c) Most haemolytic anaemias, are undoubtedly the result of red cell destruction by the malarial parasite. Certain drugs and chemicals such as sulphonamide, para-amino-phenol, and products containing lead and arsenic may cause haemolysis. Infections with streptococci, staphylococci, B. welchi and bartonelli are infrequent offenders. Snake venom is not unusual cause of haemolysis. It is likely that repeated contacts may cause increasingly severe haemolytic reactions through augmentation of cellular sensitivity.

C. Anaemias due to Iron Deficiency and Faulty Red Cell Production (Impaired Formation):

The mechanisms of haemoglobin formation and red cell production are entirely separate and a failure of either one produces its own peculiar form of anaemia. Anaemia *per se* causes tissue anoxia which is a stimulus for haemoglobin and red cell production in order that the oxygen supply may be increased to meet the metabolic need. However when these mechanisms fail anoxia persists.

1. *Iron deficiency, or hypochromic anaemia*—The formation of haemoglobin. The liver synthesises globin from body stores and dietary sources of amino acids. Globin is united with a "haeme" radical resulting from a merger of porphyrin III and organic iron, catalysed from inorganic iron in the presence of copper(?). This conversion of haemoglobin transpires in the bone marrow. The body hoards iron in the liver, spleen, bone marrow and tissues replenishing it from destroyed red cells and somewhat from the diet. This is usually sufficient to meet the needs of new haemoglobin formation. Under certain circumstances iron stores may become so depleted that normal haemoglobin synthesis is impossible and anaemia results. Haemoglobin is formed if iron is available even in the presence of hypoproteinaemia, when globin is drawn from the body's own stores, if food sources are lacking.

As iron deficiency anaemia does not affect the maturation of red cells, the total erythrocyte count is normal, or slightly reduced. In fact the bone marrow is usually hyperplastic. As the main deficiency is that of haemoglobin, the cells are pale, i.e. hypochromic, and as time passes they may often become smaller, i.e. microcytic. This state of affairs explains all the characteristic findings of this type of anaemia, e.g., the morphological aspects of the red cells in the stained smear, the low colour index because the haemoglobin is decreased disproportionately to the cell count, the normal or slightly reduced red count, the low haematocrit, a mean corpuscular volume (MCV) under 75 micrograms, and most important, a mean corpuscular haemoglobin concentration (MCHC) of under 30 per cent (normal 32-38 per cent). This is considered as a definite indication for iron therapy.

Clinically the cause of the anaemia may predominate the picture obscuring symptoms and signs of anaemia. Perhaps this is well, as it impresses the examiner with the need of treating the cause. Anaemia *per se* results in lassitude, weakness and lack of mental energy. The patients often have sore tongue, dysphagia, indigestion and intestinal upsets. Dependent oedema is common, often due to hypoproteinaemia. The skin may be dry and wrinkled, hair sparse and nails thin. Often there is cardiac dilatation with functional murmurs.

Occasionally iron deficiency anaemia may develop after a long time if the diet is low in iron, especially if this is associated with achlorhydria

preventing absorption by deficient ionisation. Iron absorption is also impaired by chronic diarrhoea. Infants on milk, which contains little iron, and aged patients on special diets are prone to develop hypochromic anaemia.

It also occurs as a complication of chronic haemorrhage when iron is lost along with the blood, depleting reserve stores so they are inadequate for haemoglobin regeneration. Hypochromic anaemia is frequent in chronic infections and nephritis wherein utilisation of iron is impared. Whatever the cause, iron therapy is ineffective until the underlying cause is removed. Iron deficiency associated with cirrhosis, has not been explained, although considering the effect of the organ on blood formation there are many possibilities. Hypochromic anaemia exists in myxoedema, and disappears as the endocrine imbalance is controlled.

Not only hypochromic but also macrocytic anaemia occurs in pregnancy. Normal pregnancy is associated with haemodilution and a "physiological" anaemia. Therefore, anaemia should not be diagnosed in pregnancy unless the haemoglobin is under 10 g. The foetus is an obligatory parasite and as it grows it steals more and more iron and protein from its mother's stores. If these have been depleted by illness, recent pregnancies, or inadequate intake, then iron deficiency, or macrocytic anaemia will appear. Iron absorption is frequently hampered by achlorhydria, so common in pregnancy. Again, many pregnant women begin their puerperium with a pre-existent anaemia. Such is the unfortunate state in some degree of almost every pregnant mother among the poorer classes. The blood picture is as described, although there may also be evidence of arrested erythropoiesis in the presence of macrocytes.

This brings us to what has been considered as a separate entity and is called idiopathic hypochromic anaemia. It is a disease of women in midlife who have borne and suckled many children. Their iron stores are deficient and achlorhydria is usually present. Very often they have been on a poor iron intake, or may have suffered from infections. They are weak, listless, complain of indigestion and anorexia which further worsen the anaemia. Usually they are invalids. Some show the Plummer-Vinson triad of dysphagia, glossitis with the anaemia. The blood picture reveals hypochromia, microcytosis and also the red count is reduced with evidence of anisocytosis. Some may respond to iron therapy if the appetite returns, but others may need an artificial menopause through irradiation, the disease usually clearing up after change of life.

Hypochromic anaemia is common in infants and children, whose iron stores are often low because of the increased demand for haemoglobin and cells to fill the ever enlarging vascular tree. In the first year of life the blood volume is doubled. Children, therefore, have a much lower reserve of iron with which to meet infections. Anaemia from haemorrhage develops much more readily in children than in adults. Most anaemias of infancy and childhood are secondary. Morphologically, the blood picture is similar to other hypochromic anaemias, although the reticulocyte counts may be higher. Whatever the cause, anaemia in childhood is a serious condition and calls for prompt treatment of the underlying condition even more than that of the anaemia.

2. *Anaemias due to decreased red cell production (megaloblastic macrocytic anaemia)*—The development of erythrocyte precursors, or normoblasts, from the primordial red cell, or proerythroblast, depends upon the presence of nucleic acid. This is synthesised in the bone marrow from amino acids only in the presence of folic acid (or Will's factor) and vitamin B_{12} (the extrinsic factor of Castle). This is absorbed from the gut only in the presence of the intrinsic gastric factor. Probably vitamin C also participates in nucleic acid synthesis. In the absence of folic acid, vitamin B_{12}, or the intrinsic factor, nucleic acid is not formed and pro-erythroblasts become abnormal megaloblasts, which produce large deeply chromatized red cells, or macrocytes.

Whatever may be the manner in which the bone marrow is deprived of one, or more, of these essential elements for nucleic acid formation, the result is the same. In each case there is an abnormal cell series in the bone marrow producing abnormal progeny in the blood stream, and also there is a retardation of the rate of red cell production resulting in low counts.

Examination of a smear of the peripheral blood shows many hyperchromic macrocytes, and a striking variation in red cell size and shape (anisocytosis and poikilocytosis). Haemoglobin is not reduced to the extent of red cell numbers, so the colour index is over one. Unused stores of iron lie idle. The MCHC is well above the upper limits of normal (38 per cent), and MCH and MCV may be increased. A bone marrow smear should be studied in each case to show the prevalence of megaloblasts. If iron deficiency anaemia coexists, hyperchromatism is lacking. A gastric analysis is indicated to determine the presence of achlorhydria.

The pathogenesis of macrocytic anaemias is dependent upon what factors have resulted in a deprivation of folic acid or vitamin B_{12}. Of all the anaemias of this group only one is not secondary to some primary cause, *i.e.* pernicious anaemia

which being rare in India will not be considered. This is due to a lack of the intrinsic gastric factor.

Probably the most common variety of macrocytic anaemias is that due to deficiency of folic acid. This is frequently due to inadequate dietary intake, making up a large group of nutritional anaemias in this country. In pregnancy, or in a growing child, the increased demand for folic acid is not met by sufficient intake and anaemia develops. In other patients with steatorrhoea or diseases impairing the absorptive function of the intestinal mucosa, folic acid is not absorbed. Probably macrocytic anaemia following gastrectomies and bowel resections is due to this cause.

Vitamin B_{12} deficiency may be due to malabsorption in the absence of the intrinsic factor, but is more likely to result from insufficient intake in the diet. Vitamin B_{12} deficiency often results from utilisation of the vitamin by aberrant intestinal bacteria, or by failure of its synthesis in the lower bowel by a change in the bacterial flora. Such is a danger from the prolonged use of oral antibiotics.

This brief review shows the extreme variety of conditions which enter in to cause the arrest of normal red cell formation. It behoves the physician to consider every possibility in searching for the responsible cause. Without treating this, therapy is merely symptomatic. Macrocytic anaemias may also be the result of bacterial, toxic, chemical, or physical trauma upon the bone marrow itself, so injuring the cells that erythropoiesis is impaired. Cancer metastases, or leukemic overgrowth may crowd out normal marrow. There usually results a decrease not only in red cells, but white cells and platelets as well.

TREATMENT OF THE ANAEMIAS

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The treatment of anaemia should be based upon an understanding of the type encountered, after which the cause should be found if at all possible. Inspite of tempting pharmaceutical preparations available, the use of "shot-gun" prescriptions is unnecessary and sloppy medicine. *A specific drug is beneficial only when it is deficient and needed.* An understanding of the type of anaemia connotes just which drug to use, and its administration should produce a remission in the form of increase in haemoglobin, red cell count and reticulocytes within a reasonable time. A failure for this to occur indicates a wrong diagnosis, inadequate dosage, or malabsorption.

A. Anaemias due to Chronic Haemorrhage and Sepsis

These are two of the most common causes of anaemia and may not present any characteristic blood picture, although reticulocyte counts may be high in chronic haemorrhage. The treatment of acute haemorrhage is obviously directed toward stopping the source of blood loss and replacement therapy by transfusion if necessary. Hematinics in the presence of chronic blood loss are at best of only temporary benefit until the leak has been controlled. As mentioned in the article on The Differential Diagnosis of the Anaemias the cause may be hidden, or due to menorrhagia, bleeding piles, hookworm, etc. It is useless to pour drugs into these patients without treating the cause. This means a careful history and examination of patients in whom the cause is obscure. Vitamin K may be helpful in arresting chronic haemorrhage if the prothrombin time is prolonged. Although the primal need is stopping the loss of blood, this does not mean that the use of iron and a high protein diet are not indicated and beneficial in patients with long standing chronic blood loss in whom such stores have become depleted.

Anaemias due to chronic infection are believed to be the result of a failure of synthesis of haemoglobin due to an inability to make use of available iron. For this reason iron therapy is ineffective, and treatment must be directed at eradicating the infection before anaemia will disappear. Recently cobalt has been used with variable results on the basis of the contention that it promotes the synthesis of haeme and globin.

B. Iron Deficiency (Hypochromic) Anaemias

The commonest iron deficiency anaemias are those associated with dietary insufficiency, increased demand for iron as in growing infants and children, during pregnancy and lactation, improper absorption in chronic intestinal diseases, after surgical alterations on the intestinal tract, chronic haemorrhage which has depleted body stores of iron and finally in idiopathic hypochromic anaemia in multipara approaching the menapause in whom iron excretion may be increased. The haematological aspects of this anaemia have been covered, and once the diagnosis is assured, whatever may be the cause, iron, and only iron, is needed. An exception is the "dimorphic" variety in which iron deficiency occurs with macrocytic anaemia wherein folic acid is needed in addition.

In theory and practice . . .

there are many signs which suggest that effective measures must be taken to prevent or overcome a nutritional deficiency brought about by inadequate intake or absorption of the fat soluble vitamins A and D.

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Although the normal daily requirement of iron is only 1·2 mg. which is met by absorption from foodstuffs, when iron deficiency anaemia occurs sufficient iron is not available in the food to make up for this imbalance, and additional iron therapy is indicated. Iron is absorbed in the ionic form, almost entirely in the upper part of small intestine. Absorption is enhanced by the presence of chlorophyll, bile pigments and calcium, and delayed by the presence of mucus. Soluble ferrous salts, e.g. sulphate, are more readily absorbed than those in the ferric form. The presence of ascorbic acid in the stomach aids in the conversion of ferric salts to the ferrous. Hydrochloric acid aids in the absorption of iron, but such is not entirely dependent upon the presence of acid in the stomach. It is likely that the therapeuic use of hydrochloric acid stimulates the appetite, but the amount given is too small to have any effect on the iron absorption.

Ferrous sulphate may cause gastric or intestinal irritation even if given after meals, in which cases ferrous lactate, or gluconate, may be substituted. The absorption of insoluble ferrous carbonate in the form of Blaud's pill is capricious and somewhat unreliable. If used, the tablets should be of recent manufacture, as with age they tend to become hard and may pass through the gastro-intestinal tract in their original form. Although the ferric salts contain more iron, a smaller per cent of iron content is utilized. All iron salts are relatively nontoxic in usual therapeutic doses, and if given after meals do not usually cause gastric or intestinal irritation. The efficacy of any iron salt is dependent upon its iron content and absorbability. The utilisation of 25 mg. of iron daily will cause a daily rise of haemoglobin of 1 per cent in severe anaemia. As normalcy is approached this rise decreases. When the need is less, the dose may be decreased. Maximal response should be attained in the course of four weeks.

Adjuvants—The use of added copper in refractory adult anaemia and those of infants and children is still not fully endorsed, but may be tried especially in infants on a purely milk diet. Copper is believed to have a catalytic action and assist in converting inorganic iron to haemoglobin. Although there are theoretical grounds for giving ascorbic acid, it seems that there is no clinical proof of its efficacy. By far the most important, and perhaps the only necessary adjuvant to iron therapy is a diet which provides sufficient protein intake to meet the demands for haemoglobin reconstruction. If such is available, the need for both porphyrin and globin constituents will be met. Patients should have approximately 80-100 g. of pure protein daily. In case there is a failure to respond under iron therapy in 7 to 10 days, it may be assumed that : (1) the diagnosis of anaemia is faulty or that it is due to infection or continued blood loss, (2) that the dose is inadequate, (3) that the iron is not being absorbed, possibly due to gastro-intestinal irritation. If hypochromic anaemia fails to respond to oral iron therapy, or if there is an urgent need for available iron, parenteral iron may be used. This is employed in the form of saccharated iron oxide, 5-10 c.c. given intravenously *very slowly*, on four successive days. Each cubic centimeter contains 10 mg. of iron. As toxic reactions may occur and because phlebitis and thromboses take place at the site of injection, the use of parenteral iron is not to be encouraged, and should be reserved for emergencies only. If such injections are repeated there is a danger of haemochromatosis, or haemosiderosis, developing. The following conditions are suggested as possible indications for parenteral iron: (1) refractory iron deficient anaemias, or those which show severe gastro-intestinal reactions to oral compounds ; (2) some cases of iron deficiency anaemia of pregnancy, especially if near term ; (3) those associated with ulcerative colitis, or rheumatoid arthritis.

Preparations and Dosage :

Ferrous sulphate—contains 360 mg. of available iron per gram of which 10 per cent is utilised. Average adult dose—0·6 g. daily.

Ferrous lactate (or gluconate)—contains 200 mg. of available iron per gram, of which 8 per cent is utilised. Average adult dose is 1½ g. daily.

Ferrous carbonate—contains 100 mg. of available iron of which 7 per cent is utilised. Average adult dose is 3 g. (Blaud's pill) daily.

Ferric et Ammon. Citras—contains 200 mg. of available iron per gram, of which 1½-3 per cent is utilised. Average adult dose is 4-8 g. daily, in mixture.

The dose schedule for children is dependent upon age, those under six roughly require about one third of the adult dose, and from seven to twelve about two thirds. For infants a syrup of ferrous sulphate may be employed in which 4 c.c. contain 0·16 g. of the anhydrous salt.

C. Macrocytic (Hyperchromic) Anaemias

This group includes anaemias usually associated with malnutrition, infancy, childhood and pregnancy ; and less commonly with gastro-intestinal disturbances due to niacin deficiency, sprue, fish tape-worm, hepatic disease, gastro-intestinal sur-

gery, and finally primary pernicious anaemia. They are the result of arrested and abnormal maturation of red cell precursors in the bone marrow due to deficiency of vitamin B_{12} and/or folic acid. The available preparations for combating this group of anaemias are:

Liver, orally—Fresh liver partially cooked will produce a remission if from 200 to 400 g. are taken daily. Dried liver concentrates, or liver/hog stomach preparations are also effective (with the advent of liver extract these are rarely needed.)

Liver Extract for intramuscular injection is used almost exclusively being an economy of time and money. Many varieties and concentrations are on the market. Patients with an idiosyncrasy to one can often tolerate another.

Vitamin B_{12} is used orally and parenterally. This is the extrinsic factor of Castle and contains cobalt. The dose ranges from 1 to 10 micrograms daily in severe anaemias, which is tapered off with improvement to maintenance doses of 10 to 60 micrograms every few weeks.

Folic acid, or pteroylglutamic acid (Will's factor)—Dose 10 to 20 mg. daily orally.

Nutritional macrocytic anaemias respond to folic acid therapy, but adequate dietary protein must be taken to supplement its use, especially in hypoproteinemia.

Macrocytic anaemia of pregnancy is now believed to be best treated with folic acid, but the growing foetus may cause a marked delay in response. If vitamin B_{12} is used, larger than ordinary doses are necessary. Liver extract seems less effective. Absorption may be inhibited and these drugs may need to be given parenterally, at least until there is a response in the reticulocyte count. As the transformation of folic to folinic acid is dependent upon the presence of ascorbic acid, vitamin C may be added empirically, although this has not been proven to be effective clinically. Here, even more than in nutritional anaemia, there is a need for sufficient protein intake to meet the needs of haemoglobin formation as well as the growing child. Macrocytic anaemia of pregnancy, and occasionally nutritional anaemia, exists with an iron deficiency anaemia revealed by a mean corpuscular haemoglobin concentration under 32 per cent, i.e. the "dimorphic" type, and iron therapy is also needed.

Macrocytic anaemia of infants responds to folic acid, and possibly to vitamin B_{12}. Ascorbic acid, 200 mg. daily, may be added to assist in conversion of folic acid.

Macrocytic anaemias of gastro-intestinal disease and after surgery are treated with conventional doses of folic acid. Response may be prolonged.

Primary pernicious anaemia is the result of an absence of the intrinsic factor, hence oral therapy with vitamin B_{12} is useless as it is not absorbed. During relapse 2-5 c.c. of liver extract first given twice to once daily, then weekly, or vitamin B_{12} 10-15 micrograms twice weekly with diminishing amounts at longer intervals should be effective. The amount needed depends entirely upon the reticulocyte response, rise in haemoglobin and red cell counts, and relief of symptoms. A reticulocyte response should occur in 2-3 days if the dose is sufficient, and normal counts reached in 4-7 weeks. The red cell count should rise about 400,000 cells per week and the haemoglobin 1 per cent per day, if original counts are low. Even though large doses of folic acid have resulted in remission, this is not the drug of choice for this condition. Life long maintenance doses of liver extract 1 c.c. every two weeks, or vitamin B_{12} 60 micrograms parenterally every 4 weeks should retain a total red count of 5 million cells per cc. which is essential for successful control. In the presence of infection, arteriosclerosis, or nervous complications, e.g. subacute combined degeneration, the dose must be doubled during relapse and probably also for proper maintenance. Although drugs may not cure the nervous symptoms, if given in adequate amounts they will prevent further progression. So satisfactory is the response to this treatment, even in severe cases, transfusions are usually not indicated except in the presence of severe sepsis.

Macrocytic anaemia in sprue is one of the most obstinate forms of anaemia encountered. Whereas in some reticulocyte response and rise in haemoglobin occur fairly readily, in others treatment may have to be continued for upwards of two months before a satisfactory response is reached. This is probably largely due to poor absorption from mucus and diarrhoea. Folic acid is the drug of choice. With much flatulence carbohydrates should be reduced. Parenteral folic acid may be tried.

D. Haemolytic Anaemias

Haemolysis occurs in a large number of clinical syndromes due to inherited abnormal cells, or acquired causes. Though the variety is great they are quite rare with the exception of anaemia following malaria. Attacks may cause such profuse red cell destruction that transfusion may be necessary to save life.

Congenital—In the case of hemolytic icterus splenectomy will prevent further relapses, but it

does not alter the underlying erythron defect. Tolazoline has been said to be effective in sickle cell (African) anaemia, but this is unproven.

Acquired—Whatever the cause, whether drugs, infection, toxins such as lead, allergy, exposure, or trauma, this must be identified and avoided if relapses are to be prevented. This is specially important as haemolysis tends to become more widespread with each successive attack. The use of cortisone, 25 mg. 4-6 times daily, for acute haemolytic anaemia has been found to be helpful in many cases, but such treatment requires hospitalisation under strict medical surveillance. Here also transfusion may be necessary and even life-saving. These not only relieve anaemia, but seem to serve as a therapeutic agent as well. Splenectomy may be helpful in acquired acute and subacute haemolytic anaemias, but should be preceded by transfusions. Iron may be used to replace loss through the kidneys in haemoglobinuria. Folic acid, vitamin B_{12} and liver are of no use. After all is said and done, there is no reliable therapy for haemolytic anaemias.

E. Miscellaneous Anaemias

Anaemias associated with liver diseases, especially cirrhosis and Banti's syndrome, respond poorly to any therapy, probably due to inadequate synthesis of proteins in the liver. They may be iron deficient, or macrocytic in character. A high protein intake and iron may help, but transfusions are often necessary. Folic acid and liver extract may be tried for the macrocytic type. The anaemia of chronic nephritis is of obscure origin and likewise fails to respond to any specific therapy. Transfusions may be necessary if they are severe, but great caution must be exercised.

Anaemias due to endocrine deficiency are usually due to hypo- or hyperthyroidism. Iron deficiency anaemia may occur with either, although macrocytic anaemia occurs usually only with hypothyroidism. Anaemia disappears when the imbalance is corrected.

Anaemias due to vitamin deficiencies are usually haemorrhagic in scurvy and vitamin K deficiency. Although adjunctive iron, diet and even transfusion may be needed, no permanent cure is gained until the underlying deficiency is corrected.

Anaemias due to bone marrow aplasia are usually associated with deficits of other cellular elements in the blood. Their causes are manifold. Treatment other than transfusion is not helpful.

Conclusion

The *sine qua non* of successful treatment for anaemias lies in determining the type of anaemia, finding its cause if at all possible and giving specific treatment for the anaemia as well as eradication of the underlying aetiology. Supportive nutritional intake in the form of protein is often needed.

SPECIAL ARTICLE

CERTAIN ASPECTS OF MEDICAL EDUCATION IN INDIA

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The main trends in a re-orientation of undergraduate medical education appear to be towards (*a*) an integration of the curriculum so as to promote the correlated teaching of the different subjects in the pre-clinical field as well as correlation between clinical and pre-clinical subjects ; (*b*) provision of opportunities to the student to widen his experience by contact with the social, economic and environmental conditions of the patient and by participation in a home care programme ; and (*c*) a shifting of emphasis from teaching to learning by the student himself.

The methods of approach towards achieving an integration of pre-clinical subjects and of clinical with pre-clinical subjects appear to vary in different medical colleges, the most advanced type of teaching being an attempt to replace compartmental instruction in individual subjects such as anatomy, physiology and biochemistry by a scheme in which principles are stressed and the teaching programme is built around "the morphological and functional characteristics of cells, organs and organ systems." Under each subject an integration of structure and function is sought to be secured by covering in the teaching programme the relevant anatomy, physiology and biochemistry. For instance, in dealing with the kidney, the teaching would "include the comparative anatomy, cytology and histochemistry of the nephron, the chemistry of renal tubular transport systems, the physical aspects of urine formation and the mode of action of pharmacological agents on the kidney." This kind of teaching is made possible by groups of teachers from different departments working together to refashion the new curricula as well as to carry out the actual teaching programme.

In the clinical instruction given to the medical student the emphasis has so far been on clinical pathology through the study of the patient at the hospital and through laboratory investigations. The need for a simultaneous study of social pathology, that is, a study of the social, economic, psychological and environmental factors affecting adversely the health of the patient is beginning to receive attention. This change is partly the result of advancing knowledge in the sphere of those sciences which throw light on human behaviour and social relationships, although their achievements may not have reached the precision which physiology and other basic sciences have attained. For instance, the light that psychology can throw on psychosomatic phenomena and the part that anthropology and sociology can play in trying to understand clearly the patient's reactions to his physical and social environment are beginning to be recognised as valuable aids to the practice of medicine. Opportunities are being developed for the student to visit the homes of patients who attend the out-patient clinics along with public health nurses. In order to broaden further the basis of such experience for both the students and members of the staff, the development of a home care programme is being promoted by a number of medical schools. The medical care of a certain number of families in a well-defined area is undertaken by the medical school and its associated hospitals, so that an integrated service is built up for this community, which includes domiciliary care and diagnostic and treatment facilities through hospitals and clinics. Such experience starts for the medical student, in Denver for instance, during his undergraduate career and is continued during internship and later into the period when he works as a resident medical officer.

The need for switching over from a process of intensive teaching to that of enabling the student to learn for himself as far as possible is receiving increasing attention. The present system tends to turn the mind of the student into a state of passivity from that of receptivity, and curiosity and initiative therefore become deadened to a considerable extent. "In real life, however, they must continuously manipulate facts—test them, compare them with others, look at them in different contexts, discover relations between them, and practise imaginative thinking." A number of methods are being tried to promote initiative and independent effort on the part of medical students. In America the allotment of free time during which the student is encouraged to take up special studies on his own initiative and, of course, with the availability of such help as he may require from his teachers is a line of development which is fairly common in all medical schools. In certain schools considerable effort is made to ensure that the use of this free time is channelled into useful directions ; in others the freedom to use it is left so completely in the hands of the student that it may well be that some do not use it to advantage. In any case, in the total assessment of a student's work during the year, the way in which he has made use of the free time allotted to him appears to be taken into account in most institutions.

An interesting experiment in University College Medical School, London, also deserves mention in this connection. The purpose is "to help the students to observe and record accurately, to understand something of the difficulties of language so that they may acquire precision in communication, to be able to weigh evidence and interpret facts and to retain curiosity and initiative while having a well stocked mind." The method adopted is called group teaching. Students are given exercises to work out individually for 20 minutes and they discuss their findings in groups of 12, one of the teachers being present not so much to instruct the students as to stimulate them, by mutual questioning and interpretation of data, to work out a solution among themselves. Dr. M. L. Johnson, who is carrying out this training of the students, considers that such group discussion stimulates the vigorous participation of students by posing problems which promote critical and creative thinking as well as curiosity and initiative.

Yet another method that has been adopted for promoting a scientific attitude and correct ways of reasoning in the minds of medical students is the compulsory teaching of statistics in medical schools. Training in statistics is of great importance to all types of scientific workers. In the first place it helps the student to develop clear and precise thinking. He begins to learn that biological phenomena, with their wide range of variability, can be understood and assessed properly only in terms of statistical concepts based on the principles of probability. Statistical methods are essential if, as a scientific worker, a medical man is to interpret the results of his own studies. In fact, if the purpose is to train the future physician as something more than a person with high technical skill in certain branches of the practice of medicine and to give him a wider outlook on his profession and a deeper interest in the pursuit of knowledge, an introduction to the principles of statistics as part of his medical education is essential. It is not intended that every medical student should be turned into an expert statistician, nor is it possible, because the training required will be of a much more arduous and prolonged character than that which can be incorporated in the medical curriculum. What is

sought to be secured should be that he should learn the general principles of statistics partly for the purpose of enabling him to approach his own scientific studies with due recognition of the need to base them on sound statistical principles and partly for stimulating clear thinking and a scientific outlook on the day to day problems which he may have to handle in the years yet to come.

The purpose of this brief reference to certain important changes that are taking place in medical education elsewhere is to ask ourselves the question whether developments of a similar nature or of other character are not necessary in India. The objectives that these countries are seeking to secure are obviously desirable for our country also. Nevertheless, a mere undiscriminating acceptance of what is done elsewhere will not be in the best interests of any country. The philosophy that defines the functions expected of the national health service will determine to some extent the type of medical training desirable for the country. For instance, in the United States of America, the spirit of individualism is so strong in almost every sphere of activity that the idea of 'socialised medicine', if I may use the term, appears to be wholly unacceptable to those who are at present in a position to influence public policy. Socialised medicine naturally implies control of the medical services placed at the disposal of the community through the public authority, while in the United States the general desire appears to be to keep governmental control at the lowest level possible. In the circumstances the opinion in that country in regard to the teaching of preventive medicine in the undergraduate medical curriculum is to confine instruction to the preventive aspects of the functions to be performed by the general practitioner, while the teaching of public health practice should be made, it is held, a specialisation to be sought in public health schools by those who have already graduated. It is for consideration whether, in India, this is the procedure that should be adopted. In our country the conditions that exist are different from those of the United States. The poverty of the people and the fact that 85 per cent of them live sparsely distributed over the rural areas of the country make it most unlikely that private practitioners will provide, within a foreseeable future, adequate medical care to the public. The Bhore Committee reported in 1946, after a careful study, that even the subsidised system of settling private practitioners promoted by State Governments over a period of many years failed to achieve the purpose in view and the Committee recommended the creation and maintenance of a full-time rural medical service, the members of which should be paid adequately and should be prevented from taking up private practice in any form. The Committee also stressed that these medical officers should perform both preventive and curative health functions, which would again necessitate, as is the custom everywhere, prohibition of private practice. Two schemes for health services that are now being developed in the country point the way towards the elimination of private practice in the doctors associated with these services. The community project scheme is helping to provide a medical service for the general public in which the doctors are called upon to carry out both preventive and curative health work and they are not allowed to take up private practice. Community projects are expected in due course to extend over the whole country, and as our financial position improves, the range of health services made available to the people and their quality will also tend to improve. Again, the medical service for workers which is being created under the Employees State Insurance Act is based mainly on a full-time service of doctors without the right to do private practice, although in a few States the panel system based on private practitioners is being asked for. It may be too early to pronounce a verdict in favour of either the full-time system or of the panel system, but such evidence as exists seems to point in the direction of the full-time system being more satisfactory. Under the Employees State Insurance Act medical care can be extended to the families of workers and this extension is already under serious consideration in view of the growing demand for it. Further, the term 'worker' can be extended to include all classes of workers, including agricultural labour. When these developments take place the medical care programme under the Employees State Insurance Act will cover probably 80 per cent of the total population of the country. Indeed, as I see it, the two types of health services, the one under the community project scheme for the general population and the medical service for workers will, at some stage, tend to converge and coalesce into each other and emerge as the national health service. As the tendency of both the services is to eliminate private practice by the doctors who are employed in them, it seems correct to assume that the future would see the development of a national health organisation in which the doctors who are employed will be required to devote their whole time to the public duties with which they are entrusted. This assumption is strengthened by the fact that our Prime Minister and Central Health Minister support these views in regard to the development of the nation's health services, which they hold should be financed in part by contributions from the people themselves.

In the circumstances that I have tried to describe briefly it seems fairly clear that, unlike U.S.A., the incorporation of training in public health practice at the undergraduate level is eminently necessary in India. This view has already been accepted by the Indian Medical Council in the recommendations it has put forward for including actual field training in a rural health centre as part of the internship to be undergone by all medical students. This practical training should, in my opinion, be supplemented by a reorganisation of the teaching programme in preventive medicine and public health for the undergraduate student, in order to shed a considerable part of what is taught about practical details regarding environmental hygiene, which is really the domain of the public health engineer, to incorporate more material in respect of bacteriology, epidemiology and public health administration and to present to the student, through participation in a domiciliary medical care programme, a fuller picture of disease as maladjustment to man's total environment, physical and social, than he is now able to obtain through a study of the patient under hospital conditions.

If the probable line of development of our national health service is on the basis I have indicated, it seems to me that the training programme of the medical student should lay special emphasis on promoting a social outlook in him, and on enabling him to practise his profession in a creative spirit. For this a useful method may be the deliberate provision, during the training period, for his active participation in medico-social work, particularly in a rural area. If such a programme can be developed without prejudice to the total content of his studies, there is much to be said for it. The programme should provide for stimulating his initiative for improvisation under the conditions that exist in our villages, for developing his powers of observation and for exciting his curiosity to explore into conditions which may lie outside what is described in text-books and class-room lectures. Instruction of this type can be organised and carried out successfully only under the able guidance and supervision of teachers, who should themselves be capable of imaginative thinking and of adequate adaptability to adjust their technical knowledge and skill to the special conditions that rural areas would present.

I have attempted to put forward certain suggestions in regard to the teaching programme with special reference to preventive medicine and public health practice, mainly because I am more familiar with that field of health activity than with other branches of medicine. But I hope I have helped to make it clear that our programme of teaching, if it is to take into account the requirements of the country, would differ to some extent from what is deemed desirable elsewhere. The proper development of a suitable curriculum for undergraduate medical students is a task which should be undertaken on the basis of wide discussion and prolonged consultations, in which the teachers and principals of medical colleges should take a prominent part. It is desirable that some of these newer methods should be tried out in individual medical colleges.

I should like to deal with this subject further. In India and in the United Kingdom statutory bodies exist for promoting the maintenance of certain minimum standards, although the universities are responsible for the detailed regulation of the courses of training imparted in the medical colleges affiliated to them. These statutory bodies are the Indian Medical Council and the corresponding body in the United Kingdom. In the United States, on the other hand, there is no such co-ordinating body with powers conferred on it by legislation. The Association of American Medical Colleges, the American Medical Association, and the Associations representing different specialities like surgery, internal medicine and obstetrics and gynaecology participate in providing the necessary stimulus for promoting improved levels of medical education. Formulation of standards is carried out through extensive work by committees and through discussions at the annual meetings of the Association of American Medical Colleges. Thus the motive force behind the improvement of standards in the United States operates from within the professional bodies themselves and not through the exercise of the powers which a statutory authority possesses for regulating medical education. One result of this may be that, while progressive schools will undoubtedly seek continuously to reach higher levels of medical teaching, the attainment of uniformity by all schools in respect of a minimum standard may fail to be achieved. Differences between the standards of the best schools and those of the schools at the bottom of the scale of efficiency may therefore tend to be high. In India what is desirable is that provision should be made for extensive discussion before changes in curricula are put forward. Some time ago a conference of anatomists met in Hyderabad city to discuss their subject, the Rockefeller Foundation having undertaken to meet the expenses of this Conference. Similar conferences of teachers of other subjects are also necessary. Further, group consultations between those who teach the different pre-clinical subjects and between those engaged in pre-clinical and clinical

teaching respectively should be provided for. The establishment of an Association of Indian Medical Colleges will be a welcome step in this connection. It can provide the forum, because its membership will include both the Principals and other teachers in medical colleges, for the discussion of all matters relating to medical education, including improvement of the curriculum and of teaching methods.

I shall now turn to some other important aspects of medical education in our country. About two years ago Dr. Alan Gregg, Vice-President of the Rockefeller Foundation, toured extensively in India for about four months, visited our medical colleges, held consultations with their teachers and also discussed problems of medical education with State Governments and their health advisers, because nearly all the medical colleges in the country are maintained by State Governments. He then made a valuable report. The more important among his recommendations are :

1. There should be a substantial increase in the pay of teachers of all grades in medical colleges.
2. The age of retirement of teachers should be raised from 55 to 60.
3. A change in the spirit and purpose of examinations for medical students is necessary.

I would add to these the need to improve the staffing, equipment and accommodation of different departments in medical colleges in order to promote efficient teaching and, what is equally important, to stimulate research.

I believe that all the medical colleges in India except four or five are maintained by State Governments. Therefore, in order to improve existing standards of medical education, the main responsibility would appear to be on these Governments. But the Government of India cannot absolve itself of responsibility in the matter. Higher education, which obviously includes postgraduate medical education, is a subject in the Union List under our Constitution. Therefore, in this field, the Centre has been made directly responsible for all the measures that may be necessary. Secondly, the Indian Medical Council Act is a piece of Central legislation and the Indian Medical Council created by it is responsible for enforcing the standards considered necessary for undergraduate medical education. The ultimate responsibility for the fulfilment of this purpose rests on the Central Government. In the circumstances the task of promoting measures for improving medical education should be taken up jointly by the Central and State Governments.

Under Article 263 of the Constitution the President has established a Central Health Council of which the Chairman is the Central Health Minister and its members the Health Ministers of the States. It is this body that should take up the question of medical education and should develop, in due course, an agreed programme of action to establish improved standards, the Centre and the States accepting the responsibility to share the cost on an approved basis. A precedent for this sharing of expenditure already exists. Under an upgrading programme certain departments in particular medical colleges have been selected for being improved in respect of staffing, equipment and accommodation in order to enable them to become postgraduate training centres not only for the State concerned but also for the country as a whole. In recognition of this the Central Government is bearing one-half of the cost, recurring and non-recurring, in each case.

In the light of these considerations the following suggestions are put forward :

(*a*) A Central cadre of teachers for medical colleges should be created and maintained. The tradition that medical education, particularly in the clinical field, should be left in the hands of honorary doctors has been too long prevalent in our country. These honorary doctors are often busy practitioners and, as they have to earn their income from such practice, they are not able, even with the utmost good will, to devote as much time as is desirable to the proper functioning of their departments. In particular, failure to develop research has been a noticeable feature. It is suggested that there should be, in each department, a core of full-time doctors who are paid reasonably adequate salaries and are forbidden private practice. On them will devolve the main functions of teaching and of promoting research in their respective fields; it is becoming increasingly recognised that an atmosphere of research is essential for improving the quality of teaching. It is not intended that honorary doctors should be entirely excluded. In fact they will prove particularly valuable for courses of lectures in special fields. On the other hand the main work of the department will fall on full-time workers. It is the posts that these men fill which should be incorporated in a Central cadre of teachers for medical colleges. It is suggested that this cadre should include professors, associate professors and assistant professors or lecturers. The Centre should bear a part of the cost of maintaining this Cadre and, taking into account this Central Constitution, the States should accept the scales of pay laid down for the Cadre and agree to make up the

difference between their own existing scales and those of the Cadre.

For the All-India Medical Institute the Government of India has already accepted the principle that all members of the staff will be full-time and without private practice in any form. The scales of emoluments that have been agreed to are higher than those prevailing in existing medical colleges and may be considered to be reasonably satisfactory. The scales of pay for clinical and non-clinical posts are the same.

Government of India have also agreed that clinics should be organised by each clinical department, that the booking of cases should be through the hospital authority, individual doctors being forbidden direct approach to patients, that the fees recovered should be in accordance with the scales laid down by Government and that the whole amount so obtained should be credited to Government. It is anticipated that a substantial sum of money might thus become available. In the past every proposal for a rise in salary has been met by the objection that Government has no money. It is expected that the income derived from these clinics would help to get over this objection.

The creation of a Central cadre will help to attract young men of talent to the medical educational field. It is desirable that, as far as possible, people should be left in particular institutions or within a group of institutions in the same place, so that they may work jointly with their colleagues and develop sound traditions of teaching and research. Exceptions may arise to this general proposition as, for instance, the lending of a particular professor or associate professor from a well-developed department in a medical college for a period of a year or two to another institution where this department is weak, in order to assist in the proper building up of the latter.

(*b*) The question of raising the age of retirement for teachers suggested by Dr. Gregg is important. It is for consideration, however, whether it should be a general raising of that age to 60 in respect of all teachers or an extension of service up to that age for those whose services are considered valuable in the public interest. Some discrimination should obviously be exercised in deciding whether it is worthwhile to extend the age limit in individual cases. Otherwise even those who are inefficient and whose weeding out would be desirable would get their term extended. Moreover, if it is made a general rule, there will undoubtedly be a similar demand from other branches of public service as well and the financial implications of such a change may prevent the acceptance of even the proposal in respect of teachers.

(*c*) A survey of existing facilities in the different departments of our medical colleges from the point of view of teaching and research is being undertaken by the Centre. The results of this study should prove important in that existing deficiencies will become focussed. Further, by an examination of the information thus collected, it may become possible to lay down certain general standards in respect of accommodation, staff and equipment for individual departments and thus provide the basis for calculating how much financial help would be needed in each case. It is hoped that, as part of the first and second Five-Year Plans, it would become possible to make available substantial financial support for improving our medical colleges.

(*d*) Mention should be made of a scheme that is being started by the Indian Council of Medical Research, in association with the Rockefeller Foundation, whereby selected teachers in different medical colleges will be helped, through fellowships, to obtain postgraduate qualifications. The Council has had, in addition, for the past few years, a programme of training teams of workers in non-clinical subjects for individual medical colleges on the understanding that the State Governments concerned would employ these teams on a permanent basis. It should be remembered that the funds of the Indian Council of Medical Research are practically all derived from grants made by the Central Government so that that Government is making a valuable contribution to these schemes.

(*e*) Dr. Gregg raised the question of examinations. A reorganisation of our methods of assessing the work of students requires serious consideration. What is desirable is that it should not be judged merely on the basis of the results of a terminal examination. It is necessary that a record of the work of the student during the year as a whole should also be taken into account in making the final assessment. In the United States the teacher takes with him on his clinical rounds only a few students, sometimes three or four, and he is therefore able to give personal instruction to individual students as well as to gain an impression about their work and ability. Moreover, the tutorial system helps in the same direction. A rise in the ratio of teachers to students and provision for more personal contacts between them through the tutorial system would be necessary in our country if the process of judging the work of students is to be placed on a sound basis.

(*f*) The measures taken for improving medical education will have to be on the basis of a continuing programme. It would therefore seem to be desirable to create suitable machinery for the purpose. A technical Standing Committee, for

instance, established by the Central Health Council will be able to study the problems of medical education and research continuously, to assist in correlating activities in the field of medical education with those of other branches of scientific study in the universities and to promote, from time to time, the changes that may become necessary in the light of the growing needs of an increasingly fuller provision of health protection to the people. The expert advice and guidance given by such a Committee will prove to be of great value to the Health Council in formulating its policy and in suggesting ways and means for the implementation of that policy. One of the functions of that Committee should be to promote active collaboration between professional Medical Associations, universities and other organisations and individuals interested in medical education.

(*g*) The lead for these advances should come from the Central Government, and adequate financial help should also be forthcoming from that Government. It may then be expected that a broad-based programme of action will be developed with far-reaching beneficent effect on medical education in this country. In order to secure co-operation from the States it would be necessary to associate, as indicated earlier, the Central Health Council with the formulation of the necessary measures and with their implementation.

CASE NOTES

ADDISON'S DISEASE—REPORT OF A CASE

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Since the publication in 1885 of Addison's classical monograph "On the Constitutional and Local Effects of Disease of the Suprarenal Capsules", hundreds of cases of Addison's disease have been reported from different parts of the world but surprisingly, as far as we know, none has been reported from India yet. The only doubtful case which Tribedi and De (1940) have mentioned, had only extreme weakness, loss of weight, but no pigmentation. There was no laboratory finding to support the diagnosis. Till recently tuberculosis of the suprarenals was thought to be much the most common cause of this disease, but the incidence of atrophy due to unknown toxin appears to have increased in recent years and it is now thought to be as common as tuberculosis. Syphilis, amyloid disease and primary and secondary metastatic neoplasm are some of the rare causes of this disease. None of the above mentioned diseases are rare in our country. Moreover malaria and kala-azar are endemic in India. That they affect the suprarenals adversely is well known, though it is not known if these two diseases have ever produced typical Addison's disease. Fraga (1914) described an adrenal form of malaria which is characterised by muscular weakness, low blood pressure, rapid pulse on standing, together with pigmentation and much depressed temperature. Many of the clinical features of kala-azar suggest deficiency of the suprarenal cortex. Considering all these the incidence of Addison's disease is expected to be high also in India, and we agree with Tribedi and De "that because of the rarity of Addison's disease, unless all the classical signs and symptoms are present, it is not surprising that the condition might be overlooked". Lack of proper laboratory facilities might also be a factor in the non-recognition of this disease.

The following case is reported with the hope of drawing the attention of the physicians in India, so that proper search may reveal more cases of Addison's disease in future.

Case Report

Patient, a Hindu widow, aged 40 years, from Banaras was admitted on the 16th November, 1953 with the out-door diagnosis of "Gastritis'. Her chief complaints were anorexia, vomiting and slight fever for 10 days which started insidiously.

She had malaria at the age of ten.

She had three issues of which two died at the age of six months.

Physical examination revealed, an adult female of average build, poorly nourished, severely anaemic, asthenic and apathetic. Though the patient was of dark complexion, face, hands and feet were darker than the rest of the body. Both the palms were pigmented and there were leukodermic spots in both of them and also on the outer side of the left foot. Pulse was 100 per minute, regular with small volume and low tension. Temperature was 99°F. The spleen and the liver were palpable 1½" and 1" respectively below the costal margin. Apex beat was in normal position, very feeble. Cardiac sounds were feeble and there was no murmur. Blood pressure was 85/55 mm. of Hg.

Blood examination showed Hb. 35 per cent (Hellige), R.B.C.—1·8 mill/cmm., W.B.C. 2,200/c.mm., neutrophils—64 per cent, lymphocytes—28 per cent, monocytes—4 per cent, eosinophils—4 per cent and no malaria parasite. Aldehyde test, Chopra's test and complement fixation test for kala-azar were negative. Sternal marrow did not reveal any L.D. body. Urine examination showed

low specific gravity (1012) but no other abnormality. Stool examination did not reveal anything abnormal.

Stay in Hospital—During the first fortnight of her stay in the hospital, the patient had several irregular attacks of vomiting and diarrhoea each lasting for a day or two for which she was treated symptomatically. Subsequently further examination revealed the following:

Pigmentation: In addition to those already mentioned in connection with face, hands and feet (including palms and soles) a deeply pigmented scar mark was found in the abdomen. Pigmentation was also noticed in the muco-cutaneous margin of mouth, mucous membrane of inner side of cheek, soft palate, sides and undersurface of tongue, around external urethral meatus, in labia minora and on the dorsal aspect of the clitoris.

Axillary and pubic hairs were sparse.

Cardiovascular system: Apex beat and cardiac sounds were feeble as has already been mentioned. Blood pressure was recorded regularly and the average reading was 85/55 and minimum recorded was 78/40 mm. of Hg. Electrocardiogram (Fig. 1, *vide* Plate) showed flat and inverted T in some of the leads (said to be the commonest abnormality, if present) and depressed S–T segment in V_5. It is said that there is no specific E.C.G. pattern of Addison's disease and about half of the cases do not show any abnormality (Somerville, Levine and Thorn, 1951).

Renal function: Specific gravity of urine was 1012 and the response to water drinking (Kepler-Power water test) was markedly low—none of the hourly morning samples of urine being greater than the overnight sample. Total amount of the overnight sample was 6 oz. only and after making the patient drink 680 c.c. of water (20 c.c./kg. body wt.). 1st hour sample of urine was 2 oz. the 2nd hour 1 oz. and the 3rd hour 2 oz. only.

Carbohydrate metabolism: (i) Oral glucose tolerance test. A flat glucose tolerance curve was obtained—the fasting blood sugar being 80 mg./100 c.c. and the maximum 100 mg./100 c.c. reached after an hour of ingestion of glucose (Fig. 2).

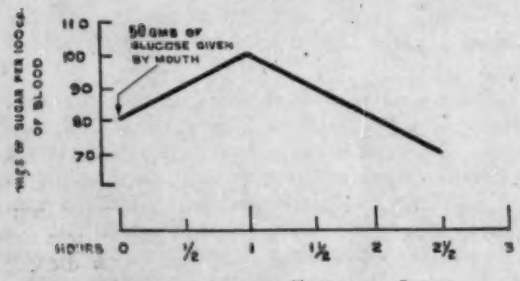

FIG. 2—ORAL GLUCOSE TOLERANCE CURVE.

(ii) Intravenous glucose tolerance test. After intravenous injection of glucose (0·5 g./kg. body wt. in 20 per cent sol. given in 30 mins), blood sugar level went upto 450 mg./100 c.c. from the fasting level of 100 mg./100 c.c. and then dropped down to 75 mg./100 c.c. within 3 hours (Fig. 3).

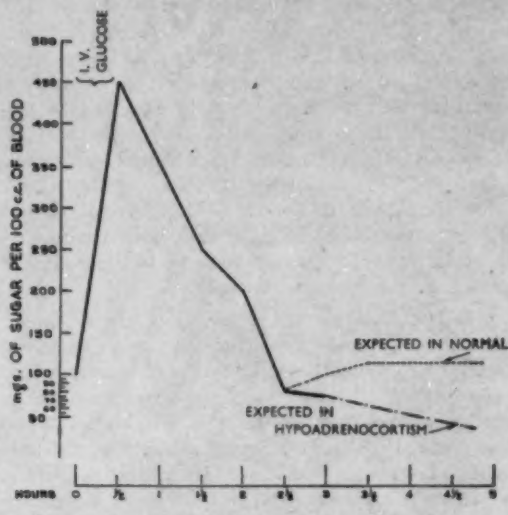

FIG. 3—INTRAVENOUS GLUCOSE TOLERANCE CURVE.

As the last two samples of blood were clotted they were not estimated (The patient's condition did not permit repetition of this test). In normal persons blood sugar level is prevented from falling to a subnormal level but in Addison's disease (though not in all cases), the fall continues to a subnormal level till sugar is given to the patient.

Plasma electrolytes—Plasma sodium, potassium and chloride were estimated and they were 287·1 mg., 19·5 mg. and 555 mg./100 c.c. respectively. Though potassium and chloride were within normal range, plasma sodium was definitely low.

Response to ACTH on the circulating eosinophils (Thorn's test): After an injection of 25 mg. of ACTH no fall of circulating eosinophils was detected after 4 hours.

Urinary excretion of neutral 17-ketosteroids: Total amount in 24 hours was 1·45 mg. only, which is much lower than the normal (4·5 to 19·5 mg. in women (Wright, 1952).

Haematological examination: A complete haematological examination showed: Hb—20 per cent (2·9 g.), R.B.C.—0·85 mill/cmm., M.C.V.—106 cμ M.C.H.—33·9 γγ, M.C.H.C.—32·2 per cent (In this case the anaemia was macrocytic and normochromic in character, contrary to the finding of Villasenor *et al* 1948).

Van den Bergh—indirect positive, bilirubin content—0·2 mg.

Sternal puncture showed normoblastic response.

Gastric analysis report was within normal limits.

Skiagrams of chest and abdomen were taken but no lung lesion nor suprarenal calcification was detected.

Tuberculin test (1/100,000 dilution) was negative.

Blood W.R. was positive.

Unfortunately the result of the treatment with common salt and cortical hormone could not be evaluated, as the patient left the hospital, soon after the institution of the above treatment.

Discussion

The symptomatology of our patient conforms to that of Addison's disease—described by Addison himself i.e. "anaemia, general langnor and debility, feeble heart action, irritable stomach, with a dingy or smoky discolouration of the whole surface . . . . . " Leukoderma, which has been found in our patient, has also been described by Addison in his monograph. Besides the above mentioned clinical features, we have based our diagnosis on low plasma sodium, low urinary excretion of neutral 17-ketosteroids, lack of response to ACTH on the circulating eosinophils and the results of the oral and intravenous glucose tolerance test. As regards the probable cause of Addison's disease in our patient, it is difficult to suggest anything except syphilis, which may be a mere coincidence. Before we conclude we must mention that we could not detect any cause of the enlargement of the spleen and the liver and the slight rise of temperature. During the course of the patient's stay in the hospital, the temperature came down to normal and both the liver and the spleen diminished in size—the latter disappearing under the costal margin. Except quinine bihydrochlor which was given empirically, there is nothing which can explain this change.

Summary

A typical case of Addison's disease, probably of syphilitic origin, is described. The authors believe that proper search will reveal many more cases of Addison's disease in India in future.

Acknowledgment

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CAPSULATED STRAIN OF PROTEUS VULGARIS

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H.M., 45 years old, was admitted in the Bowel Diseases Ward of Chittaranjan Hospitals in a collapsed state. After necessary resuscitation it was found that he had been suffering from irregular pyrexia, diarrhoea, generalised oedema, for about three months.

History of onset and present illness :—He had been suffering from irregular pyrexia, diarrhoea and gradual swelling of his body for the last three months or more without any treatment. These complaints were of insidious onset. He was a vagrant. Recently his condition becoming worse and he was removed to this hospital.

Physical Examination : He was an adult male of average build, emaciated, with oedema all over the body. He had a few pressure sores on his buttocks. Pulse—95/min., regular, volume small and tension low. Respiration—30/min. Temperature—varying between 99° and 100°F. Systemic examination did not reveal any other relevant findings.

Laboratory Examinations : Urine—Scanty, pale yellow in colour, sp. gr.—1010, reaction—acid, albumin—present a trace. Microscopically—a large number of pus cells, epithelial cells and a few red blood cells were present.

Blood : Hb—38 per cent (Sahli), R.B.C.—2·2 per c.mm., W.B.C.—8,500 per c.mm., poly—88 per cent, lympho—10 per cent, mono—2 per cent. No parasite or abnormal cell seen.

The man expired, soon after admission.

An autopsy was performed. There was no other significant finding except a huge retroperitoneal collection of thick greenish yellow pus in the right side of the posterior abdominal wall extending from the region of the iliac crest to the region of the right kidney. None of the organs in this region was involved except the capsule of the right kidney which was covered with a slough.

The pus was collected under sterile precautions and several smears were stained by Gram's method which showed plenty of pus cells and cell debris in the midst of which were seen a few gram negative bacillary and cocco-bacillary forms. These bacteria revealed a stained body and were surrounded by a clear halo around them giving an idea of the presence of a capsule round the organism. Straining was repeated by different methods and every time our preliminary observation was confirmed (Fig. 1, *vide* Plate).

Cultures were made in nutrient broth, nutrient agar and blood agar :

NUTRIENT BROTH showed luxuriant growth with thick turbid deposit at the bottom and a thin scum at the top. Removal of the plug emitted a fishy odour. Motility could not be ascertained. On staining the growth showed to be a mixed culture, predominantly Gram negative bacilli and cocco-bacillary forms and a few Gram positive cocci in groups.

NUTRIENT AGAR showed marked growth and mostly of whitish opaque confluent colonies. Staining showed almost the same picture as in nutrient broth.

BLOOD AGAR showed definitely two types of colonies. Marked haemolysis was noted round one type of colonies which were of spreading single type. Organisms from these colonies were found to be Gram negative bacilli and cocco-bacillary forms. The organisms from the other colonies were Gram positive cocci arranged mostly in clusters. They were coagulase negative.

Bacteria were separated and subcultures were made in different media again including MacConkey's medium.

After 24 hours' incubation MacConkey's medium showed opaque colonies almost covering the whole plate. The swarming nature of the colonies could be ascertained. The culture emitted a sickening fishy odour. The organisms were found to be motile and Gram negative bacilli of different sizes. Staining by Gram's method did not reveal any halo round the organisms as in the original smear from the pus.

The culture was suspended in 6 per cent (w/v) glucose solution in water and mixed with India ink. Thin films were drawn in the same procedure as with blood films, dried and fixed in methanol and stained by aqueous methyl violet or 1/10 carbol fuchsin.

Bacillary bodies were stained violet or red and the capsules were shown as clear halo against a dark back-ground (Figs. 2 and 3, *vide* Plate). This capsulated bacterium was identified as *Proteus vulgaris*.

Haemolytic property was tested against sheep's cell in the plate where clear areas round each colony was observed and in the test tubes where 0·1 ml. of a 24 hr. broth culture was added to a 5 per cent suspension of sheep's cell in saline, incubated at 37°C for 2 hours and left in the refrigerator overnight—produced complete haemolysis of the cells.

Pathogenicity test was performed in the white mice by injecting 0·2 ml. of 24 hrs. broth culture into the peritoneal cavity.

The mouse died in 7 days. At autopsy multiple abscesses were present in the abdominal cavity specially in the liver, gastro-intestinal tract, omentum and in the kidneys.

Culture of the pus from these lesions revealed similar organisms.

Thus the cause of death of the patient was evidently due to pyaemia, caused by *Proteus vulgaris* infection.

DISCUSSION

This observation of ours is interesting due to the fact that in the literature and also in the recent exhaustive work of Dugnid, capsulated strain of *Proteus vulgaris* has not been mentioned. Besides the well known capsulated bacteria, capsules have been demonstrated in *Bact. aerogenes, B. coli*, and young strain of Streptococci. This strain of *Proteus vulgaris* gave us an opportunity of studying the phenomenon of capsule formation. It was noted that capsule formation was more marked in the animal bodies. Amongst the different culture media in which the organism was subcultured capsule formation was most marked in blood agar containing a sugar in its constitution.

A comparative study of the methods for the demonstration of capsules was attempted at. A few methods that were attempted at were as follows : (1) Hiss's method, (2) Muir's method, (3) Fleming's Nigrossin method, (4) Relief staining method, (5) Method of Churchman and Emilianoff, (6) Dry film India ink method. Of these the last named elicited the best results, in our hands.

SUMMARY AND CONCLUSION

A case of *Proteus vulgaris* infection is diagnosed at autopsy. The strain of organism showed presence of capsules round them. A comparative study of the methods for demonstration of capsule has been assessed.

ACKNOWLEDGMENT

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CHANGING CONCEPTS ABOUT IDIOPATHIC THROMBOCYTOPENIC PURPURA

That spleen had a distinct role to play in the pathogenesis of idiopathic thrombocytopenic purpura was long suggested by Frank[1] and by Kaznelson[2]. Frank carefully studied the bone marrow and concluded that the essential lesion was gross structural changes in the megakaryocytes whose activities were inhibited by the spleen. Kaznelson incriminated spleen as a 'thrombocytolytic' organ which selectively destroyed platelets and produced thrombocytopenia. Many successful splenectomies performed since then amply proved the baneful influence of an abnormal spleen. In later years Doan[3] supported the conception of Kaznelson and elaborated his selective sequestration theory, while Dameshek and Miller[4] upheld the theory of Frank and postulated that megakaryocytes were inhibited by humoral factors produced in the spleen. In the main, however, all the workers were unanimous regarding the prejudicial role of spleen, the points of conflict centering round the precise mechanism of splenic action. Direct implication of these observations was the evolution of the conception that idiopathic thrombocytopenic purpura (ITP) is a form of hypersplenism.

Recent researches in the field of immunohaematology have brought forth enough evidences which bid fair to modify the above ideas. On the basis of positive Coombs test and the presence of platelet agglutinins, Evans *et al*[5] suggested that ITP was an immunological phenomenon. They coined the term immunothrombocytopenia and asserted that the basic mechanism in ITP was essentially similar to that in the immunohaemolytic anaemia. This conception was very strongly supported by the contemporary observations of Harrington *et al*[6] and Stefanini and Chatterjea[7]. In acute cases of ITP transfused normal platelets were very quickly destroyed showing thereby the active role of an extraneous factor in the causation of thrombocytopenia. Induction of consistent thrombocytopenia in normal recipients by the transfusion of plasma from chronic cases of ITP unequivocally demonstrated the presence of a thrombocytopenic factor. That the platelet destruction did not take place selectively in the spleen was proved by the further works of Stefanini *et al*[8]. Role of lungs could also be eliminated by the platelet transfusion experiments of Stefanini *et al*.[9]

Evidences suggesting the role of a thrombocytopenic factor was also provided by the studies of Epstein *et al*[10]. These workers carefully followed seven babies born of five women suffering from ITP. Six of the seven babies had transient thrombocytopenia. The transient thrombocytopenia was not influenced by splenectomy before or during pregnancy. They concluded that some humoral factor independent of the spleen was transferred across the placenta into the foetus and produced thrombocytopenia. Recent works of Harrington *et al*[11] clearly established the role of platelet agglutinin in the causation of neonatal thrombocytopenia.

By the use of specialized technique and avoidance of non-specific platelet agglutination, specific antihuman platelet agglutinins, active both against "iso" and "auto" platelets, were demonstrated by Stefanini *et al*[12] in the sera of some cases of chronic ITP. Later Dausset *et al*[13] demonstrated a thrombocytolytic antibody which needed complement for its activation. Ackroyd's [14] careful works in sedormid purpura suggest that a lytic system may be operative in many cases of drug induced thrombocytopenia. Thus all the recent observations tend to favour an auto-immune mechanism in preference to an exclusive hypersplenic mechanism. In the light of the immunological studies and from the results of a long-term follow up of a large number of cases it has been concluded that acute cases of ITP mostly represent an allergic reaction and in these cases platelet antibodies are not demonstrable in the serum. Chronic cases comprise two distinct groups—(i) an immunologic group with

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demonstrable antibodies and (ii) a hypersplenic group which do not show any antibody. It is possible that spleen may have a common role of removing platelets damaged by noxious substances or sensitized on an immunologic basis.

A perusal of recently reported cases show that immunothrombocytopenia may not be an isolated affair. In some cases there may be an associated immunohaemolytic anaemia. It is conceivable that in a similar fashion all three types of blood cells may be implicated resulting in the production of what may be called immunopancytopenia. Moeschlin[15] describes such a case. A similar example where a triple immunologic disturbance is responsible is provided by 'thrombotic thrombocytopenic purpura' (Singer *et al*[16]) where the immunologic mechanism affects red cells, platelets and smaller blood vessels (Dameshek and Stefanini[17]). In many respects the disease thrombotic thrombocytopenic purpura resembles periarteritis nodosa, a collagen disease, which is thought to be a manifestation of vascular allergy by many authorities. Haematological disturbances, particularly the cytopenias occurring singly or in combinations seen in disseminated lupus, also appear to be the result of an immunologic storm. The similarities between the ITP and collagen diseases may be explained by assuming that all these disorders are different manifestations of a common immunological disturbance, modified by the intrinsic cellular and humoral resistance of the human host.

MENTAL HEALTH

The question of mental illness has not, as yet, received recognition as an integral part of medical and economic welfare of the people. Naturally it has not found a place in the official programme of the medical and public health department of the government of this country. The position however is quite different in other countries of the world.

Our people are generally indifferent to this problem of mental illness perhaps because they think that proper treatment of it has not yet evolved. Also they try to conceal mental disorders because of the stigmata associated with them.

Besides, the human mind still remains an unexplored territory, and psychology and psychiatry are comparatively new sciences. So the intellectual people also seem to be little interested in mental illness as they think it to be medically beyond control.

From the standpoint of economic losses as well as of human misery, the role of mental health should have gained substantial recognition much earlier.

If the objects of medical programmes are to keep man alive and productive, preservation of mental health should be considered as a paying proposition. It is now difficult to say accurately as to what extent mental illness has extended in this country, due to insufficient and inefficient statistics. But it may be said without risking controversy that it is fairly on the move.

And this was the reason that led the World Health Organisation to take up this matter in 1949. It became difficult on the part of WHO to win its acceptance in the programme of major medical problems, but a committee was formed to formulate principles and recommendations based on mental medical problems as they actually existed throughout the world. It was a practical approach which might have led to practical solutions. The committee, however, due to extreme differences amongst the various countries regarding the level and scope of development of treatment facilities proposed that mental health problems should have only preventive application of psychiatric knowledge.

Pandit Nehru, our Premier, in inaugurating the seventh session of WHO Regional Committee for South East Asia emphasised the importance of mental health in modern world more than physical health. Pandit Nehru's reference to mental health should not be taken as casual. It is the result of keen observation of a penetrating mind. He wanted to initiate a new outlook on this subject without in any way minimising the importance to be placed on tuberculosis, malaria and other communicable diseases. Physical health, Pandit Nehru said, was only one aspect of total health and a relatively small part of it, because without mental health physical health would go to pieces. Our country has been indifferent to this question up till now. At least no active movement for the elimination of this class of illness either on the part of the government or the people, is visible.

We feel, the time is quite ripe to draw the attention of the medical profession and the government to this problem. We believe, mental ailments are gaining ground from day to day and will push ahead further, because of the various factors which are cropping up in the present time, hostile to the economic life of the people. Let not Pandit Nehru's observations go unheeded and let principles be formulated immediately upon which a suitable mental health programme may be based.

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CURRENT MEDICAL LITERATURE

Arterial Pressure in General Population

HAMILTON AND OTHERS (*Clin. Sc.*, **13**: 11, 1954) give in the following lines the summary of their observations on the aetiology of essential hypertension with relation to arterial pressure in the general population:

The casual arterial pressure has been measured in a sample of the general population, including ages from the second decade upwards. This sample comprised all subjects attending, on certain days, the out-patient clinics for varicose veins, diseases of the skin, orthopaedics, fractures and dental treatment.

Average arterial pressures rise with age. For systolic pressure the growth curve is curvilinear, but for diastolic pressure there is no significant deviation from linearity.

The curves relating average systolic and diastolic pressures to age differ in the two sexes.

Testing the population sample for homogeneity showed only one significant difference between its three constituent groups, namely, the more rapid rise of systolic pressure with age in females suffering from varicose veins.

Our figures closely resemble those of previous workers, except when their subjects have been selected in such a way as to bias against so-called hypertension.

Histograms suggest that there is probably considerable individual variability in the rate of rise of arterial pressure with age.

There is no natural dividing line between those with high pressure and those without. In every decade the series is continuous, and any division must be purely arbitrary.

It is suggested that what is termed essential hypertension represents not a disease entity, but merely that section of the population presenting arterial pressures higher than an arbitrarily selected value, and having no disease to which these pressures can be attributed.

Chair Rest Regimen in Acute Myocardial Infarction

WILSON AND WARD (*J.A.M.A.*, **155**: 226, 1954) write that thirty consecutive patients with proved myocardial infarction have been treated by the chair rest regimen. Among the advantages of the chair rest regimen in the treatment of myocardial infarction are: (1) lower mortality, (2) minimal incidence of complications, (3) improved patient morale, and (4) shorter convalescence with more rapid rehabilitation and return to gainful work. None of the complications occurring during treatment nor any of the three fatalities were attributable to the regimen of chair rest care.

The observations in this series of patients agree with findings of others that persons with acute coronary occlusion who are allowed to sit up in a chair receive more complete mental and physical rest, with fewer complications and a lower mortality rate as a result.

Recurrence of Mitral Stenosis Following Commissurotomy

KEYES AND LAM (*J.A.M.A.*, **135**: 247, 1954) report that a patient with severe mitral stenosis received benefit from a commissurotomy that was maintained for a period of 18 months after which there was recurrence of all of the symptoms, indicating refusion of the valve leaflets. A gratifying result was obtained by repeating the operation on the mitral valve. Although recurrence of mitral stenosis after a technically adequate operation on the valve is extremely rare, when it does occur the possibilities of a second operation or even a third should not be overlooked.

Bilateral Haemorrhagic Effusion in Acute Pulmonary Moniliasis

BASS AND OTHERS (*Lancet*, **1**: 709, 1954) in reporting on a case of acute pulmonary moniliasis developing bilateral haemorrhagic effusion as a complication observes that the condition is not very uncommon. Ikeda distinguished three main groups of pulmonary moniliasis:

(1) Mild with cough and scanty sputum.

(2) Moderate with cough, sputum, and low-grade fever.

(3) Severe with dyspnoea, night sweats, cough, sticky glairy sputum; exacerbation resembling acute lobar pneumonia; chest pains, haemoptysis.

In the case reported, the reasons for diagnosing moniliasis as put up by the authors were: (1) the absence of leucocytosis at height of the illness; (2) the absence of tubercle bacilli in the sputum; (3) the presence of *Candida albicans* in the sputum; (4) the resemblance of the symptoms and signs to those described by Ikeda as characterising the severe form of pulmonary moniliasis; (5) the failure to respond to antibiotics; and (6) the dramatic response to iodides.

Oesophageal Lesion in Scleroderma

DORNHORST AND OTHERS (*Lancet*, **1**: 696, 1954) write that in symmetrical progressive scleroderma (sclerodactyly) oesophageal lesions may produce dysphagia; it is less widely recognised that in this condition a disorder of oesophageal function is frequently demonstrable when the patient is unaware of any difficulty in swallowing.

All the six patients under review had a definite abnormality of oesophageal function: five showed the same pattern differing only in degree; the sixth had, in addition, a stricture in the region of the cardia.

The characteristic defect was failure of the propulsive waves to continue normally into the lower half of the oesophagus.

The weakness of the lower oesophagus was manifest radiographically when the patient was observed swallowing in the supine, slightly head-down, position; the bolus was carried briskly to about the position of the tracheal bifurcation where its progress ceased. A further mouthful might push it on a little, but it would not enter the stomach until the patient stood up.

The microscopic appearance is of simple atrophy with minimal fibrous replacement of the main muscle-coats in

the lower oesophagus—the muscularis mucosae is unaffected. There is no sclerosis such as occurs in the dermis.

Tuberculous Survey of Rural Areas

SEAL AND OTHERS (*Indian J. Tuberc.*, **1** : 116, 1954) give in the following lines the summary of their observations on the tuberculosis survey with the help of a mobile mass miniature radiography unit carried out in 16 villages within 2-10 miles of the industrial town of Serampore in West Bengal :

The infection and morbidity rates were found to be 38·9 and 1·55 per cent respectively. The males consistently showed higher infection and morbidity rates than the females, the ratio of the male and female morbidity rates being about 2 :1.

Analysis of the data showed that besides age this infection rate was influenced more by the nature and place of occupation, movement and contact of the people with the industrial town, than by the distance of these villages from this town.

As high as 5·2 per cent of the families were found to have tuberculous patients and 6·5 per cent gave recent history of having tuberculous patients.

The highest infection and morbidity rates were shown by the middle class families, the members of which generally have more contact with the industrial town than those of the poorer group.

Comparing the results with those of other surveys it appears that mass miniature radiography was greatly helpful in detecting larger number of cases among otherwise unsuspected individuals.

In the present state of our country, BCG vaccination may be considered as an useful measure to prevent the spread of tuberculosis, and it would be a wise policy to confine our pointed attention to the industrial towns as well as the rural areas contiguous to them. Perhaps a legislation for compulsory BCG vaccination of susceptible population, specially when they are recruited in industries from the rural areas, would considerably minimise the risk of imbibing the disease by them as well as of spreading it to others.

Bleeding Peptic Ulcer Complicating Hydralazine and Hexamethonium Bromide Therapy

MANDELBAUM AND OTHERS (*J.A.M.A.*, **155** : 833, 1954) write that more and more use of sympathicolytic drugs is being made in the treatment of malignant hypertension. The authors report a case of a 40-year old man who was admitted to the Jewish Hospital, Brooklyn, for the treatment of hypertension. After adequate investigation the patient was put on 25 mg. Hydralazine intramuscularly every 6 hours. At this time his blood pressure was 225/130 mm. Hg. After each injection the patient complained of severe pounding headache and lacrymation. After the sixth dose the blood-pressure was 190/110 mm. Hg., but the patient refused to continue with the drug. He was put on 2 doses of 25 mg. hexamethonium bromide intramuscularly at 4 hourly intervals. On the following day the blood pressure rose from 160/90 to 190/110 mm. Hg. and 25 mg. hexamethonium every 6 hours was again given. Next morning the patient passed a large tarry stool streaked with fresh blood. The haemoglobin had dropped from 15·1 g. before treatment to 9·8 g. per cent. Hexamethonium was discontinued and 2 days later a blood transfusion was indicated. Melena subsided after 48 hours and a subsequent barium meal skiagram showed considerable deformity of the duodenal cap. On inquiry it was found that the patient suffered from epigastric burning and pain after food, but these symptoms disappeared with 2 weeks of dieting and powder and did not recur. The case report is interesting as similar experiences have been recorded after surgical sympathectomy for hypertension and carries a suggestion that when hypotensive drugs are used for any new case of hypertension a milder and less disturbing agent than drugs mentioned above should be used first.

Toxic Effects of Heparin

HIRSCHBOECK AND OTHERS (*Am. J. M. Sci.*, **227** : 279, 1954) writes :

Treburon, a synthetic heparinoid anticoagulant, was given intramuscularly or intravenously to 240 patients with a variety of vascular disorders and nonsurgical diseases. The drug is an effective anticoagulant with approximately one-third the activity of sodium heparin.

Thirty-eight of the patients received a total dose of 3,000 mg. or more of the drug intramuscularly for periods of from 5 to 38 days. It was usually possible to prolong the coagulation time to between 30 and 60 minutes with a maintenance dose of 250 mg. of Treburon intramuscularly at 12 hour intervals.

Alopecia of the scalp and to a less extent of the eyebrows and suprapubic and axillary hair occurred in 19 per cent of all patients observed for the occurrence of this complication. Alopecia occurred in 35·5 per cent of all patients who received more than 3,000 mg. of the drug.

Brittle, chalky finger and toe nails, diarrhoea and epistaxis were also observed as complications of Treburon therapy.

Alopecia has also been reported as a complication following the administration of sodium heparin, Paritol-C, thrombocid and coumarin derivatives.

Corticotropin in Agranulocytosis

TAULANIEMI (*Ann. Med. Int. Fenn.*, **43** : 91, 1954) in reporting two cases of agranulocytosis treated with corticotropin observes that in the first of the cases described, it is difficult to know definitely whether agranulocytosis was due to sulfonamides or to aminopyrine-containing analgesics. In the second case, Conteben probably was responsible for the disease. In both patients the course was much of the same type, and the same applies to the response to ACTH. There was a temporary leukemoid reaction during treatment in both cases, but it disappeared when ACTH was discontinued.

The above two cases, like those previously published, support the view that, of the therapeutics used at present in the treatment of agranulocytosis, ACTH is the best as far as stimulation of granulocytopoiesis is concerned.

CURRENT TOPIC

THE CHALLENGE TO MEDICAL EDUCATION IN THE SECOND HALF OF THE TWENTIETH CENTURY*

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The title of my address has not been framed as a question, since there can be no doubt that the second half of the twentieth century offers a challenge to medical education, as indeed it offers a challenge to every variety of medical experience, to every aspect of medicine, and to the practice of medicine in every part of the world.

It is for me to examine the nature of the challenge and for you to listen in the coming week to speakers from all over the world who will make their contributions to our discussions, and who, though having in mind the general issue, will nevertheless instruct us in some of the particular difficulties of their own countries and conditions. For perhaps the first abiding value of this conference may be that we shall know more of each other and each others conditions. There can be little doubt that when we individually think of medical education we think only of our own countries.

The world, however, has now become so shrunken, because of modern communications, that we can no longer take a parochial view of our problems, whether they be economical, political, social, or, above all, medical, since medicine mercifully knows no international boundaries and happily has the same ideals in all countries. Even when countries are at war their medical professions can co-operate and be at peace one with another in a common task. Fortunately, there is a growing world-wide awareness of the common bonds of medicine and the contributions which these can make to world peace.

The World Health Organization of the United Nations and the medical offshoot of UNESCO, CIOMS, both intergovernmental in constitution, are a formal international recognition that medicine, health, science, and education present common world problems which can, in part, be faced and partially solved by men and women from different countries meeting together and expressing their views. Medical men themselves have realized the challenge by founding the World Medical Association, and I am proud to know that in this the British Medical Association has played a prominent part. The World Medical Association represents the field workers, those who have to do the job.

It would indeed be unusual, if not an indication of inertia and ill-health, if the practising doctors did not have their disagreements with intergovernmental planners. We regard the scene from different standpoints, and I can understand at least this much of Einstein's theory of relativity, that what is observed depends upon the position of the observer.

It is perhaps significant that the first great project of the World Medical Association is the holding of the First World Conference on Medical Education, and it is also significant that it has secured the willing collaboration of the World Health Organization, whilst the support and interest of the International Association of Universities can only mean that the sure foundation of medical studies is the university and the university ideal.

The first challenge which has come to the fore in the second half of the twentieth century is not confined to medical education, but is levelled at education itself, whatever calling or profession a man or a woman is to take up. The basic trouble is the same as with medicine, that the accumulation of knowledge is such as to demand early specialization and to make it impossible for a student to be comprehensive in his approach to his subject.

Abraham Flexner said that medical education was not so much a matter of medicine as of education. It is fortunate, therefore, that Sir Richard Livingstone, who has probed deeper than any of us into the meaning and purpose of education, has paid us the great compliment of coming to address a gathering of doctors and to give us the benefit of his wisdom.

It is also fitting that Professor Fulton, who has made the physiology of the brain his special study, should follow Sir Richard Livingstone and speak on his other special interest, that of medical history, telling us of the back-ground of the theme of the conference under the title of "The History of Medical Education."

And then, several thousands of miles from New England, Colonel Mallick comes from Pakistan to speak on the parting of the ways between the medicine of this century and before that time. Is medicine a technology or a profession? And if the answer is clear, as I think it is, then how must we educate youth to respond to the challenge implicit in this conception of our common faith?

In preparing for any calling there are challenges from three directions. These are directed at the teachers, at those they teach, and at what they teach. These aspects therefore form the basis of three of the main sections for the Conference, whilst the fourth, preventive and social medicine, reflects our enhanced consciousness of its importance and of its potentialities both in the medical profession and among the general public, including their elected representatives in the governments of the world.

Social medicine, not to be confused with socialist medicine, is indeed our main contact with the laity, since it covers a part of medicine which they can readily understand, and the execution of it, particularly from the financial angle, lies in their hands. In this field of medicine, too, the fundamental principles are the same in all parts of the world, whether the conditions be civilized or primitive.

* From the proceedings of the First World Conference on Medical Education. Published under the auspices of the British Medical Association by the Oxford University Press.

What is the challenge to the student? There are certain qualities essential to all students, from whatever part of the world they may derive. It is not difficult to draw a brief pen-picture of the ideal medical student: cultured, broadly educated in the humanities, intelligent and intellectual, of transparent integrity, humane and sympathetic, and, above all, one who will love his profession as well as his fellow men and all their weaknesses, their joys, and their sorrows.

It would be impossible for all students to attain such an ideal, but all should have some at least of these qualities, either inherent or capable of development, for I personally believe that unless this is so the man will never make a doctor, however well he is taught. Selection therefore becomes of importance, and will be a part of our discussion.

It is reasonable to suggest that the profession of medicine, being recruited from the upper one-third stratum of the normal distribution of intelligence, should be composed of something better than a high average. This view must necessarily be related to the demands of other professions and occupations, which likewise need to be recruited from the same stratum. Indeed, it may be necessary to survey the man-power available in relation to the number of doctors required by the various peoples, some countries being prosperous and urbanized, others prosperous and rural, many poor and underdeveloped.

In all countries it is important that the medical profession, while being technically competent, should also have such intellectual and social prestige and such unquestionable integrity as to command respect in the councils of the nation, the province, and the community. Medical students must be recruited on individual qualities and ability, quite independent of family, of personal fortune, of class or family distinction, save that a cultured philanthropic family tends to foster desirable qualities.

There can indeed be little doubt that the first challenge to medical education at this time is the challenge to education itself. Has the government of a particular country so ordered its educational system that a proportion of its youth will be fit to take up the most exacting profession in the world? If this is not the case, then the omission may need to be rectified at adult phase, perhaps in another country, otherwise there is little point in making fine or even coarse adjustments in the medical curriculum if the soil is not fit to receive the seed.

Just as we think of the ideal medical student (though we ought really to think of the average, for this is the type with which our educational methods have to contend), so also we can picture the ideal medical teacher, whether he be teaching at the beside, in the out-patient department, in the operating theatre, in the laboratory, in the lecture-room, or in the field.

Not all can attain the ideal, and it is not necessarily true, in fact often not so, that an expert in his subject can readily hand on his knowledge to others. Yet the expert and the artist can usually impart something which the professional teacher cannot convey. There is, however, much to be said for the wide use of some form of tutorial system in the teaching of medicine. By this I do not mean what is generally implied by a medical tutorial—namely, question and answer in preparation for an examination. I think, instead, of the relatively young, experienced, keen member of a hospital staff to whom a small group of students can be permanently attached during the whole time of their hospital learning. The group could gather with the tutor, once or twice a week, from their several and different duties and discuss with him the doings and experiences of the week. Such a tutor, who might well be a general practitioner, could direct studies, review the work of the week, integrate and co-ordinate the various experiences, and given point and emphasis in such a review to all the aspects of medicine, social, hygienic, psychological, ecological, historical, and so on, which various advocates would especially wish to have inserted into an already overloaded medical curriculum. Such a tutor would indeed help to correct the departmental attitude which tends to over-emphasize a narrow subject. Good tutors are difficult to find, and they should not be overloaded with too many students, otherwise the personal atmosphere, that of a family rather than a tutorial class, would be destroyed.

Presentation is in many ways as important as what is presented. The classics, thought by many to be the ideal form of education, are worse than useless if presented to the student in a way which repels him.

The selection and appointment of future teachers might well be more deliberate than hitherto, in order that some may be chosen for their teaching capabilities; and such appointments in some grades might be for limited terms instead of for life.

So much, then, for the medical student himself and his teacher. I must now take up the third challenge—namely, what is the student to be taught. From the narrow point of view one can argue endlessly whether this or that subject should be included in the curriculum and how many hours a week or a term should be devoted to it. With such an approach this conference would probably make little progress even if it were to confine its attention to the problems of the various medical schools and faculties in Britain.

Obviously the content of the curriculum is important, and during this week we shall learn a lot from each other with regard to it. Medical education, however, in any one area must to some extent be related to the medical needs of the population of that area. For example, the doctor practising in Britain will not need to be an expert in tropical medicine. Yet Britain's world-wide responsibilities in the Commonwealth have been reflected in the fundamental contribution made to the subject of tropical medicine by British workers. I need mention no more than Manson, Ross, Bruce, Leishman, and Leonard Rogers. This illustrates at least the fact that medical education can never be parochial.

The approach I have made with my programme committee has been to determine four principal sections and to select topics within these which will bring out and illuminate principles and methods. Let us

just look for a moment at a few of the many things in which a medical student might be profitably instructed or of which he at least ought to have some knowledge. The complexity and variety of the subject arise from the enormous accumulation of knowledge during the past fifty years, and especially the last twenty-five years.

Nuclear physics, colloid science, and enzyme chemistry have provided us with new instruments of thought and practice. The bacteriologist has come to govern the surgeon in the operating theatre, the nurse in the ward, the cook in the kitchen, the practising doctor who uses antibiotics, and the public health worker who is concerned with community infections. The problems of blood transfusion, at one time seemingly simple, are now an affair of genetics, specialized serology, and statistical analysis. Even clinical experience and a flair for diagnosis can no longer be regarded as infallible guides to ultimate clinical truth: the opinion needs to be checked by means of which the clinician may be profoundly ignorant. The clinician may indeed be momentarily embarrassed when asked for a quantitative expression of his observations and deductions. Medicine is coming to draw even more heavily on the more exact basic sciences and to become more precise and scientific in the formulation and execution of its tasks. It has been said that "science is measurement", and the medical statistician is now an indispensable member of the team which assesses the results of new remedies in a clinical trial or the efficacy of a new immunizing agent.

The challenge to our universities and medical schools is a simple one. Are we preparing our students at least to grasp the principles behind all this scientific work? Does the student leave the university with an understanding of the methods of science and with some knowledge of its history? The doctor of the future will have to be grounded more firmly in the basic sciences than was the student of twenty or thirty years ago, otherwise he will not be prepared to meet the challenge of advancing knowledge which is making medicine a more complete science. And here at once we come up against a difficulty. Because of the length and the ever-increasing complexity of medical studies university authorities ask that the boy at school shall have passed his first medical examination in the basic sciences of chemistry, physics, and biology before he enters the medical faculty. Parents, too, approve of this requirement because of the cost of medical education. The schoolmaster has had to bow the knee to this necessity. But there is evidence that there is now some poverty of mind in the finished medical and science graduates because of lack of general education in the humanities, literature, language, history, philosophy, and the arts. There is little doubt that the medical student who is to be a practising doctor should understand the world in which his patients live, and should be able to approach them as human beings with a depth of understanding that can come only from an appreciation of civilized values. We are indeed aware of the obvious dangers of too early specialization in science among those who are going to graduate in science and medicine. Perhaps the discussion between schoolmasters and doctors at the Conference will help to find an answer to this problem. Here, however, I would say that it is not advisable to extend the graduate period of education if it can be avoided.

It is also desirable, wherever possible, to preserve the continuity of education in school, university, and, indeed, in postgraduate studies. For example, the inorganic and organic chemistry at school should lead to extension of these subjects in the first medical examination and so to the biochemistry and physiological chemistry of the second medical examination, and thence to the application of these to the clinical work of the bedside in the form of chemical pathology. I shall listen with interest to hear whether speakers will state at which point in a student's education at school and university a medical orientation should be given, for example, to the teaching of chemistry.

From the undergraduate standpoint the depth to which the subject should be taught also presents a problem. How much chemistry? How much physics? How much anatomy? Does the intending and practising doctor need to memorize in detail, and then forget, the three-dimensional relations of the posterior triangle of the neck? Does he need to learn the dosage in Rontgen units of the radiation treatment of carcinoma of the cervix? Does he learn anything, as a student, when spending hours in an operating theatre watching the surgeon remove a tumour of the brain? Could he not spend his time more profitably in the out-patient department, the casualty reception, the polyclinic, or even in an art gallery or on the football field?

Sometimes a subject may become a burden in a particular medical school because of a struggle to maintain a department in a prominent position. I myself believe that a student should receive continuous and lengthy instruction only in the common and basic and useful and everyday clinical problems, but he should content himself with a single experience in rare or specialized procedures. The brain operation which I have quoted will serve as an example, and likewise with the highly specialist work of the ophthalmic and other departments. On the other hand, more experience in such special departments as dermatology would be repaid in the field of actual practice.

Only by discussing such views and exchanging ideas shall we eventually find out how to unload the medical curriculum to make room for new subjects and how to give more attention to parts of training that have been neglected or should receive a fresh emphasis.

I should like once again to emphasize the need for continuity of teaching and how important it is to avoid presenting the student with separate blocks of instruction, the one block being unrelated to the other except in terms of successive examination which have to be passed. The student must never think of the various phases of his education as a vista of obstacles between him and his final qualification, to be overcome as soon as possible and, once overcome, to be forgotten.

Some of the themes for discussion this week remind me of one of my most distinguished predecessors at Cambridge, Sir Clifford Allbutt, who protested eloquently and with learning against the separation of medicine and surgery, a separation for which physicians are much to blame. Likewise many now hold the view that physiology and anatomy should be integrated as a single basic subject in the curriculum. We do not now need to train the nineteenth-century prosector. He can train himself after he has qualified.

Integration is indeed a fundamental requirement in the curriculum. Teaching has grown up piecemeal. Some aspects are mere survivals which have long lost their relative importance; others, of modern conception, have not been fully appreciated or orientated. Someone might well attempt to write a reasonably short textbook giving the principles governing the integration of all the many facets of medicine. If all the bees could be collected in one bonnet we should indeed have made progress. Happily the clinician in the wards is now accustomed to welcome to the bedside the physiologist, the pathologist, the radiologist, and especially, the general practitioner.

I feel sure myself that the properly chosen medical tutor could contribute so very much to real integration and do away with both piecemeal instruction as well as the danger of disproportionate departmental and sectional emphasis.

This country's experiment with a National Health Service is one manifestation of the view that medicine is also a social science. The illness of one person is not an isolated event having no effect on others. Tuberculosis is not caused only by the tubercle bacillus. Housing, nutrition, conditions of life and work all play their part, whilst in the chain of recovery the physician, the surgeon, the pathologist, the radiologist, the sanatorium, the public health officer, and the social worker in the home and in industry are all involved.

The study of man in relation to his environment, human ecology is the fundamental basis of what is now called social medicine. The challenge to medical education to meet this growing consciousness of the importance of social medicine comes from within as well as from without the medical profession.

A complete section of this conference is concerned with the teaching of preventive and social medicine, a subject in which the World Health Organization takes a special interest. Thus, there will be opportunities for educationists from all parts of the world to exchange ideas and experiences. And it is to be hoped that what is said will help those responsible for medical education in countries where facilities are less highly developed, especially, perhaps, in the fields of social and preventive medicine.

Whatever be taught to the student, it is as well at some phase to ask ourselves coldly and critically. What is the object of undergraduate medical education? The short and incomplete answer is to turn out some one fundamentally equipped to be a practising doctor. The period of training should not be specifically directed towards the training of a general practitioner or a specialist or a public health official or an administrator, but should provide the student with a foundation for his after-career in any branch of medicine. It is his postgraduation apprenticeship and narrower studies which finally complete his early education in the branch of medicine he elects to follow, whether this be general practice or a specialized field.

The undergraduate teacher should aim at producing an educated person grounded in principle and method, able to see what the whole of medicine stands for and means, trained to observe with his hands and his senses, encouraged to think logically and critically, instructed in the use of the instruments of measurement, and equipped with a basic knowledge upon which he will continue to build for the rest of his professional life.

Are we as medical teachers doing this? Or is teaching just a by-product of our professional life? Do we positively examine ourselves from time to time with a critical eye, or do we complacently content ourselves with no more than getting the student over an examination hurdle?

Are we also satisfied with the means by which a student's competence to be qualified is assessed? Has the examination a hampering effect on what is taught and learned, and, if so, can we suggest any alternatives? Always we have to bear in mind that in many countries the manner of assessing competence and the standard are governed by law. There is, however, little doubt that experiment would show some ways in which the perpetual orthodox examinations could be advantageously modified.

Those of us who had the task of devising the programme for this Conference had to pack a great deal into the short space of a week. Many themes I should like to have heard discussed have had to be omitted. Many here might have made different choices. All of you will, I hope, by the end of this week conclude that we have made a useful beginning in tackling this most fundamental of all medical questions—education. And if that is the conclusion, I hope that, individually and collectively, you may decide that the organizations which you represent might be asked to repeat the Conference in four or five years if it is felt that that would carry the matter further.

In the meanwhile what likelihood is there that something will be done? That those in control of medical education will really have the humility and courage to admit that all is not at its best in the best of all possible worlds, their worlds? That those who hold the shaping of the future in their hands will fashion it with vision and imagination so as to inspire the young man and woman to pursue the tasks of our great profession with a feeling of dedication to something greater than themselves? There is indeed a likelihood, otherwise so many of us would not have met here in London in the month of August. But the possibilities must be turned into probabilities and certainties, and until this happens we must possess our souls with that discontent that has been so aptly called divine.

We may aim higher than we can reach. But if we aim high we shall at least reach somewhere. Our individual and collective responsibility as a profession grows, and will grow. We cannot escape it. Medicine to-day demands much from character, intellect, and practical ability, and medicine also provides a wide variety of opportunity for all kinds of talent. But talents will be wasted or misused if the structure and content of medical education are faulty, and if medical educationists remain complacently satisfied with themselves and their methods.

NOTES AND NEWS

Premier Opens Polio Clinic in Calcutta

The Prime Minister formally opened the B. C. Roy Polio Clinic and Hospital for Crippled Children in Beliaghata, Calcutta, on November 3, 1954. He also laid the foundation stone of a new building planned for the hospital. The ceremony was attended by a large number of doctors and other invited guests.

Addressing the gathering, Shri Nehru said that he had been greatly pleased when he was told about the starting of the polio clinic in Calcutta. It marked yet another stride forward in the efforts not only of this country but of the world to fight this dreaded disease. He was the more pleased because in the midst of the numerous problems that were now confronting India and her population of over 300 million souls, they had not forgotten the welfare of their children and "a nation that looks after its children must fare well". This was a motto they should always keep before them. Wherever he went in the rural areas he was confronted with the sad spectacle of suffering children, ill-clothed, ill-fed and without proper facilities for education and recreation. Such conditions were bad enough when they affected adults; they were more pitiable in children because they represented the future India.

Medical Council Discuss the Lot of Teachers

Dr. C. S. Patel, President of the Medical Council of India, pleaded for the creation of conditions in which medical teachers would be free from financial worries and be able to accept teaching as their life's work. Addressing the 42nd session of the Council he said unsatisfactory service conditions were one of the causes of deterioration of standards of teaching and training in medical colleges. Large numbers of medical teachers resorted to private practice to supplement their income and also to keep in contact with the public on whom they would have to rely after retirement. It was his view, that full-time medical teachers should be paid adequately and debarred entirely from private practice in the interests of medical education. He suggested frequent inter-university exchanges of teachers with a view to improving and maintaining uniform standards in medical colleges. He suggested the creation of an all-India cadre of teachers of medical colleges, and also giving the universities control over the appointment of, at least, professors and heads of departments.

Medical Conferences in India

Conference of Psychiatrists of India—The Annual Conference of the Indian Psychiatric Society will be held in Lucknow from 23rd December 1954 to 25th December 1954, just before the All-India Medical Conference to be held at Lucknow on the 26th, 27th and 28th December 1954.

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Conference of E. N. T. Surgeons of India—The Seventh Annual Conference of the Association of Otolaryngologists of India will be held under the presidentship of Dr. R. V. Rao at Amritsar in East Punjab from 24th December 1954. The Governor of the East Punjab will open the Conference and the Minister of Health will inaugurate the Scientific Session.

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Conference of Surgeons of India—The 16th Annual Conference of Association of Surgeons of India will be held in Hyderabad (Dn.) on the 29th, 30th, 31st December 1954 and 1st January 1955. The main subjects for discussion are:

(1) Behaviour of the urinary bladder in spinal paraplegia; (2) Tumours of the salivary glands; and (3) Cleft palate.

Further details may be obtained from Dr. A. Venugopal, Hony. Secretary, 164 Poonamalle High Road, Kilpauk, Madras 10.

* * * * *

Obstetric and Gynaecological Conference—The 8th All-India Obstetric and Gynaecological Conference which was announced to be held in New Delhi during December has been postponed *sine die*.

* * * * *

Indian Science Congress—The Indian Science Congress will be held in Baroda from 2nd January 1955. Prof. S. K. Mitra is the President of the General Section. The Medical Section will discuss "Medical Education".

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Conferences of Physicians, Paediatricians, Neurologists and Cardiologists—Annual Conference of the Association of Physicians of India, Association of Paediatricians of India, Neurological Society of India and Cardiological Society of India will be held in Nagpur on the 4th, 5th, 6th and 7th of February 1955. A symposium on 'Pericarditis' under the auspices of the Cardiological Society will be held. Further details may be obtained from Dr. J. N. Berry, Organising Secretary, Nagpur, M.P.

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Indian Paediatric Society—The Annual Conference of the Indian Paediatric Society will be held in Lucknow in February 1955.

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All-India Ophthalmological Conference—The 16th All-India Ophthalmological Conference will be held in Bombay in the first week of March 1955. The conference is devoting its scientific session to a symposium on Diseases of the Lacrimal Apparatus. It also plans to hold scientific and trade exhibitions of ophthalmic interest. Further information can be obtained from Dr. V. V. Gupte, 19, Ph. Mehta Road, Bombay 1.

CORRESPONDENCE

The Editor is not responsible for any views expressed by correspondents

Streptomycin in Bubonic Plague

SIR,—Reference 'streptomycin in bubonic plague" (*J. Indian M. A.*, March, 1953, p. 250). Being the first person to use streptomycin in human plague (Karamchandani and Sundar Rao, 1948 and 1949), it should have been my privilege to feel elated at the results achieved by Dr. Dubey. But caution is needed. Therefore will you allow me to voice a criticism? Absence of laboratory investigation is a vital missing link in the chain of his results which, in the present era of scientific approach to problems, is *sine qua non*. Besides certain species and groups of bacteria appear liable to become resistant to antibiotics, and those possessing the rapid one-step streptomycin pattern of resistance, constitute a definite clinical problem. In a fell disease like plague to toy with one gram dose of streptomycin, injected once in 24 hours, is taking a very great risk. It is now recognised (Gould, Bowie and Cameron, 1953) that all the individuals in a bacterial population are sensitive not to one particular concentration but rather to a range of concentration, which may be narrow or wide. The aim in therapy should therefore be to subject the organism to a level of concentration which is as close as possible to a bacterial level, operating uniformly during all the 24 hours. This is negatived by one twentyfour hourly dose.

It is therefore necessary that we should stick to the dosage and procedure recommended as safe by the pioneer (Karamchandani, 1951 and 1950). I am etc.

Salisbury Park, Poona 1.

P. V. KARAMCHANDANI, M.B., F.R.C.P., LT. COL., I.M.S. (RETD.).

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KARAMCHANDANI, P. V. and SUNDAR RAO, K.—*Ibid*, **1** : 22, 1948.

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Sudden Deaths

SIR,—I am extremely thankful for your reply in connection with my previous letters of enquiry to Dr. George Da Silva of Jubbalpur, our past President, on the correspondence 'Sudden Deaths' (*J. Indian M. A.*, **23** : 184, 1954).

Many of these silent and most unostentatious deaths are due to 'coronary occlusion' not necessarily thrombotic.

Dr. Da Silva has given us all aspects of this condition. Since 1927 I have been watching the condition and I had an autopsy done on the body of a college student, who died in sleep. The autopsy revealed that both the coronary arteries were occluded and the heart weighed over 16 ounces.

Later on by ECG examination at intervals, measuring cardiothoracic ratio and following up to the post mortem table I brought the facts to my seniors in profession.

I have studied the literature on the subject since 1929, I have noticed some ECG tracings with temporary changes in the S-T segment. During the early part of the World War II, I showed some hearts collected from the morgue after the coroner's verdict of natural death was declared. I exhibited them at a meeting of the Calcutta Medical Club.

I am interested in problems associated with all aspects of narrowing of the lumen, cholesteremia and calcification that have been observed and reported.

I shall feel highly thankful if you publish in your correspondence column this letter of mine. One feels the necessity of post mortem examination to add to our knowledge of such problems, I am etc.

Calcutta

J. N. MAITRA, M.SC., M.B.

REVIEWS

Resection—Reconstruction of the Hip Arthroplasty with Acrylic Prosthesis.—By Jean Judet, Robert Judet, Jean Lagrange and Jean Dunoyer: Edited by K. I. Nissen. E. & S. Livingstone Ltd., Edinburgh and London, 1954. Pp. 151. Illustrations 101.

The monograph translated and edited by K. I. Nissen, gives an accurate account of hip arthroplasty with acrylic resin prosthesis. The authors have fully endorsed the pitfalls in the manufacture of choice of prosthesis with almost mathematical accuracy. They have stressed the difficulties, dangers and short and long term complications. Proper choice of cases is essential and the method has been used for primary and secondary osteoarthritis, non-union of femoral neck fractures, congenital and acquired dislocations and subluxations and septic arthritis with varying results dependent on the indication and the age of patient.

The authors have not claimed the method as the ultimate answer but pointed out that the acrylic composition has two advantages—(a) Tissue tolerance and (b) Stability of prosthesis in bone. The monograph will be a useful guide to all surgeons interested in this type of work.

Die BCG—Schutzimpfung.—By Prof. Dr. Med. Rolf Griesbach. Publisher: Georg Thieme Verlag, Stuttgart, 1954.

The contribution of H. Spiess, Gottingen gives an exhaustive survey about the historical development of BCG from the point of view of the experimental research worker, some references permit further penetration into the subject which is well outlined in the text. The bacteriological aspects of BCG are dealt with by F. Van

Deinse (Paris). Very stimulating is A. Wunderwald's contribution on the clinical problems of BCG. Rosemberg (Sao Paulo) brings forward interesting data on oral BCG in man. Three more contributions of van Deinse (BCG vaccination in cattle; arguments against BCG and survey of the world literature on results of cutaneous BCG—the latter together with Griesbach) add to the value of the book which allows for quick and competent information of the non-expert but which is sure to be appreciated also by the critic expert for it covers a multitude of aspects in an excellent and scientific manner.

Management of The Newborn.—By A. H. Parmelee, M.D. First edition, 1952. The Year Book Publishers, Inc., Chicago, U.S.A. Price $7·00 postpaid.

This book has been written by an experienced professor of paediatrics the material being largely drawn from his own experience. Written with a personal, clinical approach, rather than in an abstract encyclopaedic manner, the book unfolds itself like the continuous chapters of a big storybook. The book is amply illustrated with a list of references at the end of each chapter for the more inquisitive reader. This book is likely to be of service to undergraduates and practitioners alike in enabling them to understand the "normals" about the fulltime or the premature baby; and thereafter to help them to take up and manage the unhealthy sick baby or the baby with various congenital disabilities.

Office Gynecology—By J. P. Greenhill, B.S., M.D., F.A.C.S., F.I.C.S. Sixth edition, July, 1954. The Year Book Publishers, Inc., Chicago, U.S.A. Price $7·75 postpaid.

This book first made its appearance in 1939 and the last, the fifth edition came out in 1948. Appearing after six years, this sixth edition has naturally had to be thoroughly revised and many chapters entirely rewritten. During these few years of its existence this book has earned a good reputation, to continue and also to enhance which several new chapters have been usefully added, mainly with the help of writers having special knowledge and aptitude in their respective subjects. Running to a total of 517 pages, it is written in a lucid style and contains a mass of informations and advice. Should be on the bookshelf of every practitioner who has to do gynaecological work—entirely or even only partly.

History of Indian Pharmacy.—By S. P. Srivastava, M. PHARM., Lecturer in Pharmacy, Department of Pharmaceutics, Banaras Hindu University, with a foreword from Dr. George Urdang, PH.G., D.SC., NAT., SC.D., Director, American Institute of the History of Pharmacy and formerly Professor of History of Pharmacy, University of Wiscosin, U.S.A. Price Rs. 12/8/-=$2·50.

To have a perfect knowledge of a thing, one must be acquainted with its past life. No knowledge can be complete without a clear conception of its evolution. The "History of Indian Pharmacy" will amply contribute to a fair knowledge and understanding of the pharmacy indigenous to the soil of this country from the very dawn of the Indian civilisation.

The book has been divided into ten chapters. The introductory one deals mainly with the qualifications of a pharmacist and his relation with the physcian, the meaning of prescription, etc. The second chapter (Mythology) describes how Ayurveda was composed by Brahma and then propagated to Daksha and then to Ashvini Kumars, Indra and others. The third chapter (pre-Charaka period) shows how charms, spells and sorcery, etc., were used as remedial measures. In this chapter the method of preparation of Somarasa has been mentioned and compared with Iranian "Homa". The first Medical Conference on Indian soil took place during this period.

In the Charaka period (4th chapter) Sushruta and Charaka became very important Indian pharmaceutical personages. They compiled Sushruta and Charaka Sanhitas, the two excellent contributions of the time to medical literature.

Post-Charaka period (5th chapter) is the time between the Vedic period and the Budha. Takshila was the most famous seat of learning in India. The great personages such as Patanjali, the philosopher, grammarian and scientist and Nagarjuna, the great chemist made their appearance at this time.

In the mediaeval period (6th chapter) Rasayana or Hindu Alchemy took a definite form and many books on Alchemy such as *Rasaratnakara, Rasahridaya Rasarnava*, etc., were compiled. They began to know the utility of metals such as mercury, gold, silver, iron, copper, etc., in the realm of pharmacy and medicine and used them in relieving human diseases and sufferings.

The 7th, 8th and 9th chapters give descriptions of Indian drugs, pharmaceutical preparations (iron pill, tonic, alkalies, etc.), pharmaceutical processes (boiling, fermentation, distillation, etc.), pharmaceutical aids and appliances (mortar, pestle, balance, measure glass, etc.), weights and mensures. Directions for collection and storage of drugs also appear in these chapters.

India's pharmaceutical contributions, the relationship of India and her influence on other countries as regards medicine and pharmacy have been given in the last chapter.

There is a large number of printing mistakes for which the author had to add a page of corrigenda at the end. The book should be used not only by all students of medicine but specially by the students of pharmacy and pharmacology. It is time that history of medicine should form part of students' curriculum in all medical colleges and certainly for post-graduates. The credit of publishing this book should go to Professor M. L. Schroff at whose inspiration and guidance the book has been written and we congratulate Sree Srivastava for the valuable contribution. This volume certainly should find a place in the library of medical institutes.

Behandlung Innerer Krankheiten.—By Prof. Dr. Ferdinand Hoff. 5th Compl. revised Edn. Publisher: Georg Thieme Verlag. Stuttgart, 1954.

This new edition has been revised in many aspects, some chapters were re-written in collaboration with Prof. Hoff's present coworkers in Frankfurt. The numerous novelties in therapeutics which became fashionable since the last edition of this book appeared, are adequately discussed, in proper balance with well established therapeutic measures of older days. The book will be of great use not only for students, but even more so for practitioners. One cannot help being impressed by the sound and clear judgment of the author in evaluating therapeutic results and this is perhaps the most educating aspect of the book.

OBITUARY

Dr. M. S. Wagle

Dr. M. S. Wagle of Gadag (Karnatak), a prominent member of the Gadag branch, I.M.A., died on 15th September 1954, after a brief illness. Dr. Wagle originally belonged to Vengurla in the Ratnagiri District. He was educated in Bombay. After passing L. M. & S. in 1912, he set up practice in the town of Gadag. In 1940, he was elected the president of the Gadag branch I.M.A. and continued in this position upto 1950. He was the president of the 11th Maharashtra and Karnatak Medical Conference in 1950.

In social life, he was associated with various public institutions. His death is mourned by a wide circle of friends and acquaintances.

May his soul rest in peace!

YOUR QUESTION

Correspondents should give their names and addresses (not necessarily for publication) and include all relevant details in the questions which should be typed. Questions of medical interest only will be acceptable for this section. They should be sent in a separate envelope marked "Your Questions." Questions of general interest will be published in preference. Lack of space precludes answering of all the questions received.

Infantile Cirrhosis

Q. What is the present-day treatment of infantile cirrhosis?

Ans. The aetiology is still a clinical puzzle. There is no specific treatment. The real treatment is preventive. Children born of vegetarian families are particularly prone to this condition. Dietetic inadequacy in both mother and child, specially the deficiency of protein, is of importance. The treatment is unsatisfactory. In early stages a change in diet and of place perhaps gives the best results. Fat is detrimental, and therefore is best altogether omitted. Carbohydrate in easily assimilable form and proteins 1·5 g. per kg. body weight are suitable. Milk is the best food, and is best given as skimmed milk. Relief of troublesome symptoms should be aimed at. Associated gastrointestinal disturbance is best treated with frequent small feeds of diluted citrated milk—or skimmed milk with 1-2 ounces of fruit juice per day. Medicinal treatment is of doubtful value. Recently on the hypothesis of some existing gastrointestinal infection, oral administration of streptomycin sulphate is being tried with encouraging results in some. Concomitant parasitic infection should have to be treated. Vitamin B complex and ferri et ammon citras or ferrous gluconate are always beneficial.

XXXI ALL-INDIA MEDICAL CONFERENCE, LUCKNOW

The 31st All-India Medical Conference will be held at Lucknow on the 26th, 27th and 28th December, 1954. The Working Committee of the Indian Medical Association will meet on the 23rd and 24th December, 1954 and the Central Council on the 24th and 25th December, 1954. An Exhibition will be held on the occasion and a Souvenir will be published. Applications for reservation of stalls in the Exhibition and advertising space in the Souvenir should be sent to the Hony. Secretary, Lucknow Branch, I.M.A., Cantonment Road, Lucknow.

Delegates and visitors wishing to attend the Conference should apply to the respective Provincial Secretaries, I.M.A., or to the General Secretary, Reception Committee, All-India Medical Conference, Charbagh, Lucknow, for the necessary certificate on production of which at the nearest D.T.S. Office, single fare double journey concession authority slip for any class will be obtained. Concession tickets will be issued by the railway booking office against production of the slip.

Delegates and visitors are also requested to bring proper warm clothing, full bedding and mosquito nets. Boarding charges will be approximately Rs. 8/- per day. Intending delegates and visitors should communicate to the General Secretary, Reception Committee, the date of their arrival at Lucknow, before the 18th December, 1954. A copy of this intimation should also be sent to the respective provincial and local branch secretaries.

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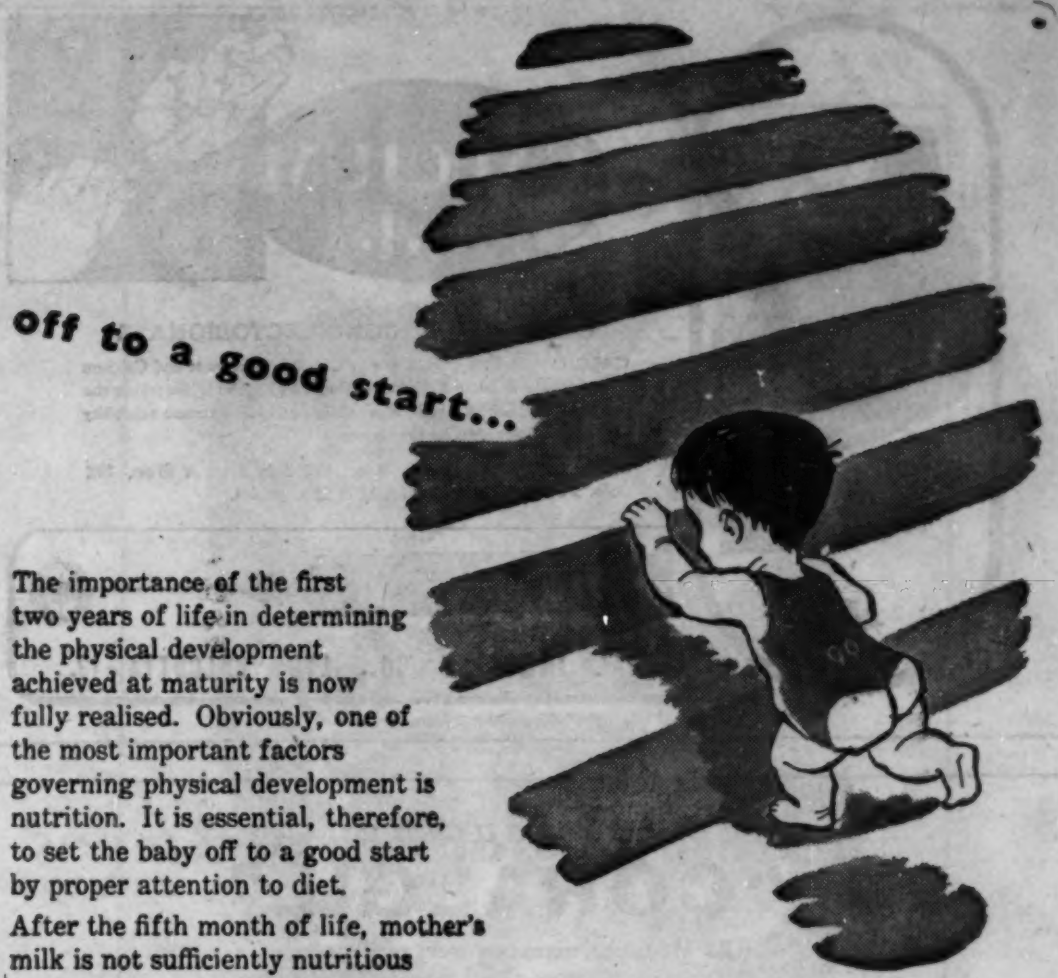

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CALCIUM B. I., a double salt of Calcium Gluconate and Calcium Lactobionate (Calcium Galacto-Gluconate) quickly increases the ionisable Calcium in blood. Has two advantages—extreme solubility and better utilization by the tissues.

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Folic Acid	1·5 mg.	Proteolytic Enzyme	10 grs.
Vitamin (B_{12})	400 I.U.	Amylolytic Enzyme	5 grs.
Riboflavin (B_2)	0·5 mg.	Lipolytic Enzyme	5 grs.
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INDICATIONS :

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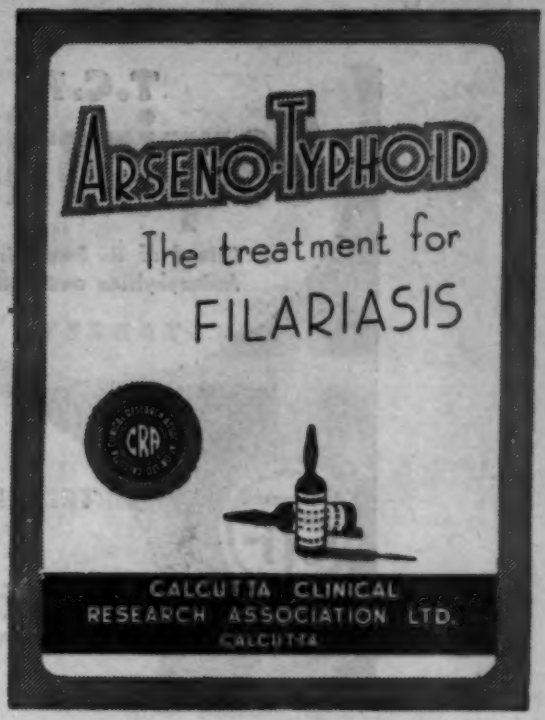

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Indicated in pregnancy, lactation, periods of rapid growth, febrile conditions, Old age convalescence and debility states, in Haemorrhagic & development of teeth & bones.

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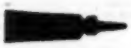
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Bacterial and virus pneumonia
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Venereal infections
Surgical infections
Gynaecological infections
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